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Brown, A. B. (1845). *Rev. Neurol.*, 168, 427.

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THE JOURNAL OF
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TRAUMATIC DILATATION OF THE CEREBRAL VENTRICLES

BY

D. W. C. NORTHFIELD

(RECEIVED 8TH APRIL, 1943)

CASES of traumatic dilatation of the ventricles may be separated into three groups although any one case may belong to more than one group.

1. Local bulging of the ventricle which in extreme degrees presents the appearance of a diverticulum. This condition will not be discussed, because the atrophy of the brain and the formation of a cerebral or meningo-cerebral cicatrix which may result from focal contusion and laceration of the brain rest upon a firm foundation of fact, of unequivocal observation.

2. The enlargement involves the whole of one lateral ventricle; it may occur on that side of the head which received the blow, or on the opposite side. These cases may provide a link connecting the processes leading to local bulging, and those causing general symmetrical dilatation. It is tempting to assume that a large focal contusion can lead to œdema of the whole hemisphere. If this were proven, and if the œdema alone, as opposed to any vascular disturbances which cause œdema were sufficiently severe and enduring, then doubtless gliosis and atrophy would lead to ventricular enlargement. Although such an explanation is accepted by many, an œdema of this extent has not yet been satisfactorily proven. The occurrence of contralateral enlargement seems related to contre-coup effects, but the precise mechanism of dilatation is not thereby explained. Raised intracranial pressure by itself cannot be the cause, unless a softened state of one hemisphere allows its ventricle to dilate.

3. General symmetrical enlargement of the lateral ventricles; rarely the third and fourth ventricles are involved, although not to any considerable extent. Two questions immediately present themselves. What is an abnormally large ventricle, and what is the incidence of the condition? Davidoff and Dyke (1937) measure the distance between the outermost limits of the bodies at the lateral angles as seen in the antero-posterior projection and regard 3·5–4·5 cm. as normal. Robertson (1941) proposed virtually the same diameter, and his figures are comparable. Evans (1942) proposes the ratio of this diameter to the transverse diameter of the skull. These methods of measurement are of help when used with identical film-target distances, but they do not take into account variations in size according to age, nor do they give due weight to those lesser degrees of enlargement in which there may be only slight increase of the lateral diameter, but considerable rounding of the angles and deepening of the body of the ventricle. The incidence of ventricular dilatation is unknown, and will remain so until encephalography is performed on every case of head injury; such a thorough investigation is not likely to be attempted. Every case would need to be done or at any rate cases with symptoms persisting more than twenty-four hours, in order to get a correct perspective, for personal observations suggest that even in clinically mild injuries slight dilatation may occur. Such figures as are available relate only to selected cases.

Peter Bielschowsky (1928) described a series of 106 cases of head injury investigated in Foerster's Clinic at periods after the accident of from several months to years. They were highly selected by reason of abnormalities of the cerebrospinal fluid system which were present to a varying degree in all. Of 48 cases of the so-called post-contusion syndrome in which there were no focal signs of cerebral damage, 77 per cent. showed abnormal encephalograms comprising for the most part various degrees of dilatation. In 38 cases in which focal signs were also present—and in those the injury was probably more severe—there were 87 per cent. of abnormal encephalograms. In a third group of 30 cases of traumatic epilepsy there were also 87 per cent.

In my own cases of head injury, no attempt has been made to gauge the frequency of ventricular dilatation as the utilization of encephalography was somewhat haphazard, but a few cases have been selected to illustrate certain points.

Case 1.—B. aged 34 years: Canadian soldier. 28th March, 1942, rendered immediately unconscious by a fall down two flights of stone stairs. Half an hour later, at 11.10 p.m. B.P. 140/100. Plantars ↖↖. Right pupil dilated and fixed. Laceration of occiput; X-rays showed fissure fracture left occipital bone. At 1.0 a.m. stertorous breathing. B.P. 245/120. Almost unresponsive; pupils, right larger than left, no reaction; moves limbs; spasms of extensor rigidity; tendon jerks all exaggerated, plantars ↖↖. C.S.F. pressure 200 mm. bright red fluid (2½ million red cells per cu. mm.).

2.0 a.m. Operation: exploration for right extradural hæmorrhage—none found. Tense brain—subdural and subpial bleeding; right ventricle tapped with difficulty (i.e. compressed) but left ventricle easily entered; blood in ventricles. Right subtemporal decompression performed. Gradual recovery.

29th March, 1942. C.S.F. pressure 400 mm. and reduced to 120 mm. fluid bloody, decompression tense.

30th March, 1942. C.S.F. pressure 210 mm. and reduced to 100 mm.

1st April, 1942. Responding to voice. Lumbar puncture difficult to perform, thought to be due to low C.S.F. pressure.

2nd April, 1942. Decompression only slightly bulging.

6th April, 1942. C.S.F. pressure 130 mm. 60 mgm. per cent. of protein.

6th May, 1942 transferred to Canadian Hospital, and subsequently graded category C. Slight increase of tendon jerks on right side. Right pupil larger than left with poor reaction and limited upward movement.

Diagnosis: contusion of right hemisphere and mid-brain.

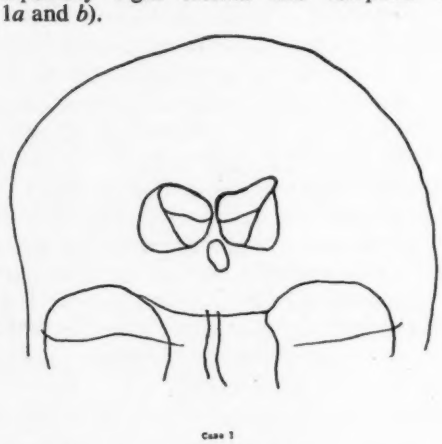
Encephalogram: enlargement of lateral ventricles, especially right frontal and temporal horns (Figs. 1*a* and *b*).

(I am indebted to Colonel Botterell, R.C.A.M.C., for the subsequent history of this man and for permission to publish the tracing of the encephalogram.)

The clinical findings pointed unmistakably to a mid-brain contusion and operation yielded good evidence of a right hemisphere contusion. But encephalography demonstrates considerable general cerebral atrophy, especially of both frontal lobes. His intellectual capacity is unimpaired, for he is back in the Service as an electrical engineer and he has no anosmia. The blow struck the back of the head. Thus there are good grounds for postulating a bifrontal contusion, but no unequivocal clinical evidence that this actually occurred.

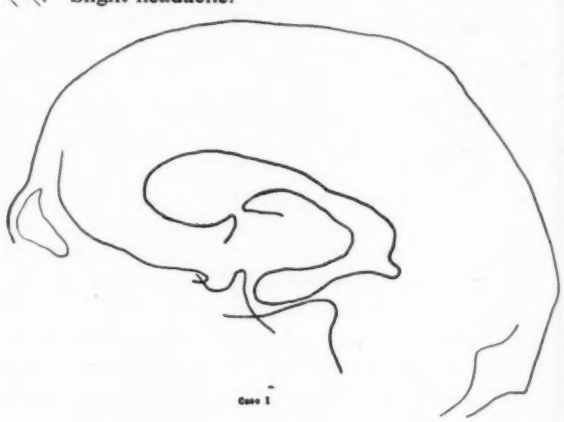
Case 2.—G.J. aged 45 years: night watchman. 6th October, 1940 admitted with " signs of cerebral irritation " to Middlesex Hospital, having been found at bottom of flight of stone steps. B.P. 100/85. X-ray: fracture left parietal running into sagittal suture and right occipital suture with separation. There was a period of mental confusion and of euphoria and he was discharged on the 18th January, 1941. He stated that he was a watchman in building in Holborn which was bombed. There was a history of fits but details were not forthcoming, except that the woman he lived with stated that he seemed well until the bombing.

22nd January, 1941 fell unconscious in street—admitted to London Hospital and transferred next day to Chase Farm Hospital. He was then drowsy and dysarthric, with ptosis, impaired upward movement of eyes, and slight left-sided spastic weakness. Plantars ↖↖. Slight headache.



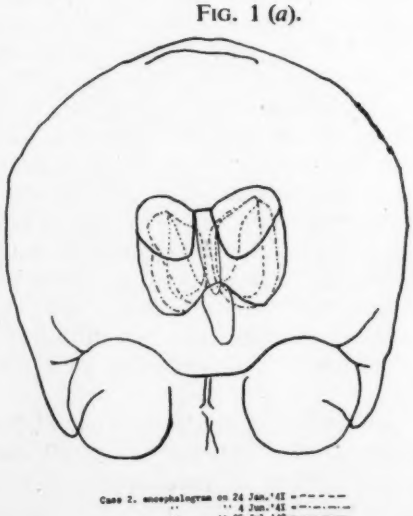
Case 1

FIG. 1 (*a*).



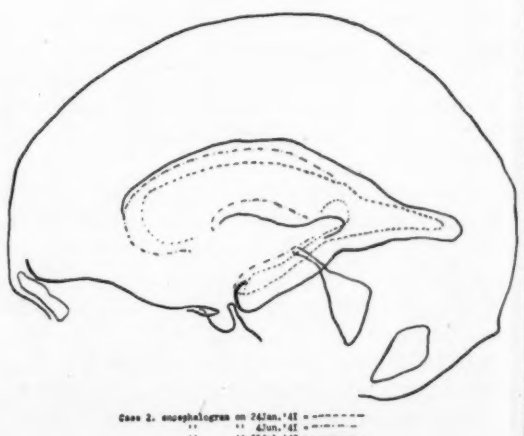
Case 1

FIG. 1 (*b*).



Case 2. encephalogram on 24 Jan.'41 = = = = =
'' '' 4 Jun.'41 = - - - -
'' '' 25 Jul.'42 ———

FIG. 2 (*a*).



Case 2. encephalogram on 24Jan.'41 = = = = =
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FIG. 2 (*b*).

C.S.F. sitting, pressure 70 mm. (fluid could not be obtained in lateral position), pink; pale yellow supernatant fluid; 9 white cells, with red cells and 60 mgm. per cent protein.

24th January, 1941 encephalogram—left ventricle larger than right, query right-sided subdural hæmatoma (Figs. 2*a* and *b*).

19th February, 1941 headaches; dysarthria; nystagmus; left plantar now flexor.

20th February, 1941 Encephalogram—slight exaggeration of former appearances. C.S.F. yellow, still high protein. *Small right subdural hæmatoma evacuated*, less than 1 oz. Slow recovery; with dysarthria and residual left-sided weakness.

May, 1941 delusions of grandeur; confabulation; eccentric but reads paper. Orientated in space and time.

21st May, C.S.F. pressure 110 mm. 1 cell and 50 mgm. per cent. protein.

4th June, 1941 Encephalography—generalized dilatation of ventricles including the fourth ventricle (Figs. 2*a* and *b*).

25th July, 1942 Encephalography—great degree of ventricular dilatation (Figs. 2*a* and *b*).

Now: euphoric. No relatives or friends and could hardly with safety be sent out to fend for himself. Helps in wards and goes errands. B.P. 120/80. Vessels soft. No retinal arteriosclerosis; slight weakness left upper limb; all tendon jerks exaggerated, bilateral extensor plantar responses. C.S.F. 1 cell. 30 mgms. per cent. of protein.

Although satisfactory details of the accident are lacking, this case is of importance because of the radiological evidence of slowly progressive ventricular dilatation, associated with prolonged mental defect which has latterly improved. The available information as to his former mental acuity is scanty but he seems to have earned his own living which he could not do now. The small subdural hæmatoma was incidental and can hardly have influenced the main clinical picture.

The next case is of a somewhat similar type.

Case 3.—S.S. aged 48 years: boiler repairer and scaler. 6th October, 1940 knocked down by car and transferred from another hospital without any clinical records six days later.

12th October, 1940 varying degree of traumatic delirium and stupor. Skin injuries around right temple and orbit. Neurological examination normal, except brisk tendon jerks. B.P. 140/85. Moderate thickening and tortuosity radial vessels. No retinal arteriosclerosis. Tongue dry. No fracture of skull.

14th October, 1940 C.S.F. pressure 60 mm. 2 cells and 100 mgm. per cent. of protein. W.R. negative. Fluids taken poorly.

27th October, 1940 C.S.F. pressure too low for satisfactory recording—faintly bloody.

28th October, 1940 C.S.F. pressure 195 mm. query bleeding due to lumbar puncture.

14th November, 1940 one month after accident mental state improving but much confabulation and disorientated in space and time.

9th January. Three months after accident encephalography demonstrates large ventricles and capacious subarachnoid spaces (Figs. 3*a* and *b*); protein in C.S.F. still high; 60 mgm. per cent.

May, 1941 euphoric; no initiative; poor memory; sits about vacantly (wife's description). Has started light employment, sweeps floors and gets tea, etc. for his "mates." No physical stamina. Mental arithmetic fair.

20th July, 1942. Encephalogram—pressure 100 mm. (taken while lying in lateral position). Still high protein in C.S.F. 70 mgm. per cent. Mental impairment. Great amount of air in subarachnoid spaces over convexity; greater degree of ventricular dilatation (Figs. 3*a* and *b*).

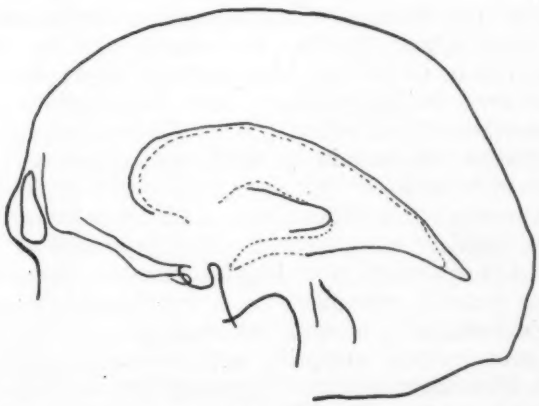
Like the previous case there has been a slow increase in the size of the ventricles over a period of eighteen months, the dilatation is fairly symmetrical and diffuse with an enormous amount of cortical air. The injury was insufficient to fracture the skull and was apparently applied to the right lateral frontal region. Although there is some thickening of the radial arteries, the retinal vessels are healthy and the blood pressure is normal. There was a prolonged period of traumatic delirium and confusion and there is still a moderate mental defect, but the man can just earn his living. Headache was rarely experienced, and the measured pressure of the cerebrospinal fluid never raised.

The next case demonstrates the difficulty of deciding whether the ventricles are of normal size or not. Although measurements and proportions are approximately normal as judged by the criteria given above (the transverse diameter is 4 cms. and the ratio 0·26), yet to an accustomed observer, the appearance is one of slight dilatation.

Case 4.—M.M. a big woman of 35 years fell heavily on her buttocks. She was not apparently rendered unconscious, but had severe headache shortly afterwards

Case 3. encephalogram on 8/Jan./'41 = — — — —
" "20/Jul./'42 = ————

FIG. 3 (*a*).



Case 3. encephalogram on 8/Jan./'41 = ·····
" "20/Jul./'42 = ————

FIG. 3 (*b*).

and was kept in bed. Some days later her headaches increased and she showed transient weakness of the left limbs. These symptoms cleared and then headache returned. A subdural hæmatoma was suspected and the encephalogram was performed some five weeks after the accident; the pressure was not raised and the fluid was of normal content. After a further period of rest the headaches disappeared and she resumed her normal home life, but she remained susceptible to bouts of headaches of a migrainous type.

It is a common experience, and supported by published cases, that the degree of ventricular dilatation is usually greatest in those patients who have sustained severe injuries, as judged by such criteria as prolonged unconsciousness, presence of focal signs of cerebral damage, temporary traumatic dementia, etc. and the presence of blood in the cerebrospinal fluid. Not only is the cerebral damage severe, but the prolonged disturbance of consciousness and mental function may mean a widespread or diffuse disturbance of neuronal function. The widespread nature of neuronal paralysis, and its longer duration when the force producing it was increased, was emphasized by Denny-Brown and Russell (1941) in their experiments on acceleration concussion. Confusion of the lesion of concussion with that of contusion is not intended, but a parallel may be drawn; namely that the process leading to dilatation of the ventricles may well be due to a generalized effect on the brain, although its microscopic pathology has not yet been identified.

Broadly speaking the possible mechanisms which may lead to dilatation of the ventricles after injury can be divided into two groups, although in practice it is possible that both may be operative in any given case. The ventricles may dilate as a result of some disturbance of the cerebrospinal fluid system; or they may dilate as a result of some change taking place primarily in the brain tissue, leading to its shrinkage, i.e. hydrocephalus ex vacuo.

Disturbance of the cerebrospinal fluid system might arise from excessive production, delayed circulation, or impaired absorption of the fluid. An excessive production can only be of significance if the production rate is greater than its absorption rate, and from the evidence available (Greenfield, 1936) this seems highly improbable provided always that the absorptive mechanism is undamaged. There appear to be no observations on the human as to the rate of secretion in head injuries, or even in the normal. Hoff (1930) performed experiments on animals in which an inspection window was made in the skull, over a tunnel in the brain leading into the ventricle. After an intravenous injection of fluorescein, a blow was struck on the animal's head. He describes the result as of clouds of pink fluid welling up from the depths of the ventricle presumably from the choroid plexus, which, however, he could not see, and further waves emanating from along the walls of cortical vessels. In their examinations of recently injured brains, Rand and Courville (1931) observed changes in the choroid plexus which they ascribed to an excess of fluid being passed into the ventricles. Thus there is some suggestive evidence of increased production and the problem deserves more careful attention before it can be stated as fact that increased fluid production does not occur.

Delay in the circulation and absorption of the fluid has been investigated more fully. Bagley (1928) showed that small quantities of blood introduced into the cerebrospinal fluid system of dogs produced matting of the lepto-meninges, scarring of the cortex, and in some cases dilatation of the ventricles. Fay and Winkelman (1930) are said to have demonstrated similar changes in cases of human brain injury and also changes in the Pacchionian bodies, but these observations need confirmation, especially as the granulations are not the only sites of arachnoidal villi. In infants suffering from hydrocephalus secondary to birth injury, matting of the lepto-meninges and retention of blood pigment can be demonstrated. We do not know whether such occlusion of the lepto-meningeal spaces is permanent, or whether in course of time fresh spaces are opened up, comparable with the canalization of a venous thrombosis. Clinical experience lends some support to the view that blood may act in this way, and in all three severe cases quoted, the fluid was bloody, but unfortunately for the argument, the amount of blood was greatest in the first although the ventricular enlargement was only moderate. Hydrocephalus is not a characteristic feature of recurrent subarachnoid bleeding from aneurysms. If such an obstructive element were active then the cerebrospinal pressure should be persistently raised, but in cases of head injury the pressure if raised usually remains so only for a few days after the injury, and it is not known whether the ventricles remain permanently dilated after a transient intracranial hypertension.

In the series of cases of Bielschowsky already referred to, this matter of delayed fluid circulation was carefully investigated. He stated that in 54 per cent. of all the 106 cases studied, the pressure was over 200 mm. Seeing that these measurements were made months and years after the injury, the proportion seems amazingly high. Somewhat similar results were published by Gierlich (1936). It is difficult to reconcile these findings with personal experience, and although Bielschowsky's paper came from Breslau, it is unacceptable without further confirmation. He also made tests upon the rate of absorption of the cerebrospinal fluid, using the iodide method of Foerster. There was a marked delay in 58 per cent. But this aspect of the problem becomes more complicated when we consider the result of encephalography. In some cases, the cortical subarachnoid spaces are not filled with air, and their occlusion may in fact have taken place. But in many cases a great quantity of air spreads over the cortex, so that occlusion cannot have occurred. We need to know whether there is impairment of the absorptive powers of the villi in such cases. Analysis of Bielschowsky's series shows that there were 28 cases of extensive collections of

air over the cortex and in 17 there was delayed absorption according to the test of iodide excretion.

It appears therefore that there is some evidence to support the view that disturbances of the cerebrospinal fluid system may lead to traumatic ventricular dilatation, but that the clinical and histological observations need further confirmation, and that investigation of the rates of secretion and absorption of cerebrospinal fluid in the normal and the traumatized must be obtained before the hypothesis can be accepted as fact.

We have next to consider whether the ventricles dilate and whether the cortical subarachnoid spaces enlarge, as a result of shrinkage of the brain substance due to change occurring primarily in the brain tissue. Here we pass more than ever into the morass of conjecture, shibboleth, and unsubstantiated observation. The view favoured by most writers is that there is a generalized œdema of the brain, which leads to gliosis and atrophy. This may be so, but critical analysis provides few if any facts to support it. Does an œdema of the whole cerebrum, or of all of one hemisphere, ever occur as the result of trauma? No records have been discovered of any histological preparations of serial sections of the whole cerebrum, or of a sufficient number of widespread samplings of brain to substantiate this claim. On the basis of his histological studies, Courville (1942, 1937) believes that generalized œdema occurs; on the other hand Greenfield (1942) states that in 31 traumatized brains, he has never seen a generalized œdema, and that the œdema has been restricted to an area some few cms. from a focal contusion. Estimations of the water content of the brain have been made, but either the methods have been unreliable, or the samplings of the brain tissue have been too few. In a recent paper Courville (1942) disinters the descriptive terms of "wet brain" and "dry brain," used at times by surgeons and pathologists alike. These terms are picturesque but mean nothing and have no scientific value. The writer has not seen, or has not recognized, such conditions at post mortem. At operation on a case of head injury one nowadays usually sees no more of the brain than is exposed by a burr hole and an opinion of the state of the brain as a whole can be of no value at all. Very occasionally one performs a subtemporal decompression and this is usually on account of focal brain contusion in the course of exploration for hæmorrhage. It is not suggested that generalized brain œdema has no existence, but it must be recognized that its actuality has not yet been proven.

There are certain observations of a different nature which merit attention. Reference has already been made to Hoff's experimental cerebral trauma. He found that some four to six minutes after the injury, the cerebrospinal fluid pressure began to rise, and this coincided with vaso-dilatation and with efflux of clouds of fluorescein. At this stage autopsy revealed a somewhat dilated ventricle. If the experiment were prolonged the intracranial pressure gradually fell and after a period of some twelve hours, the ventricles were found to be small, there was said to be œdema and fluorescein staining of the brain especially marked around the ventricles. The ependyma was found to present a number of fine tears and folds. In the light of the experiments of Denny-Brown and Russell (1941) these observations appear open to criticism, but Hoff's experiments may be classed as illustrative of compression-concussion and contusion, as opposed to acceleration-concussion. Denny-Brown and Russell did admit vasodilatation, and a rise of pressure in states of contusion; and the duration of their experiments was much shorter than those of Hoff's. Hoff argued that an outpouring of cerebrospinal fluid causes transient dilatation of the ventricles, and thus by leakage through a damaged ependyma might give rise to œdema. Gierlich (1936) reports 45 cases of brain injury, in which death occurred up to fourteen days after the accident; he describes defects in the ependyma, and hæmorrhage, hyperæmia and perivascular bleeding under the damaged and intact ependyma. These changes were parallel with the clinical severity of the injury. Rand and Courville (1931) also described changes in the wall of the ventricles, vacuolization of the ependymal cells, raggedness of the free cell margin and subependymal œdema. He interpreted these findings as demonstrating an outpouring of fluid into the ventricle from its wall, but the reverse may be actually the case. Finally, Greenfield (1942) has noted changes about the ventricle wall in cases of rapid hydrocephalus, which he attributes to a seepage of the fluid through the ependyma into the brain. These isolated observations seem to form a pattern, or at any rate a mosaic, and suggest that perhaps in severe trauma there is a temporary excessive outpouring of fluid from the choroid plexus, which by reason of a transient delay of circulation and absorption owing to the presence of blood, and aided by a traumatized ependyma penetrates the wall of the ventricle to enter the brain tissue, impairing its nourishment and causing œdema and thus to gliosis.

Summary

The cause of traumatic ventricular dilatation remains unidentified, and in endeavouring to solve the problem, hard facts concerning the following items need to be ascertained.

1. The normal size of the ventricles, and its variation with age; the incidence of traumatic dilatation.
2. Observations on the rate of secretion and of absorption of cerebrospinal fluid in health and after trauma to the head.
3. Whether blood in the cerebrospinal fluid leads to permanent impairment of its channels and its absorptive organ.
4. The occurrence or otherwise of a generalized form of brain œdema.
5. The histological picture of traumatic dilatation.

The weight of evidence indicates some change

occurring primarily in the brain tissue, leading to a degree of atrophy. But it is quite possible that more than one mechanism may operate.

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THE EFFECT OF GALVANIC EXERCISE ON DENERVATED AND RE-INNERVATED MUSCLES IN THE RABBIT

BY

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(RECEIVED 22ND OCTOBER, 1943)

IN a previous paper (Gutmann and Guttmann, 1942) it was shown that galvanic exercise of denervated muscles to a great extent counteracted the atrophy of the paralysed muscles and accelerated return to their initial volume after re-innervation. The principle of the method employed was to elicit vigorous contractions but to avoid nociceptive reactions. Stimulation was applied for 20 minutes daily with a current strength of about 5 ma.

Recent literature on the effect of electrotherapy is still found to be contradictory. Fischer (1939), Solandt (1942), Solandt *et al.* (1943) and Hines *et al.* (1943) have reported favourable results. Eccles (1941) has shown that in disuse atrophy faradic stimulation decreases the weight loss considerably. But negative results have been reported by Chor *et al.* (1939) and Molander *et al.* (1941). Chor *et al.* (1939) even claimed that the beneficial effects of massage and passive movements were lessened rather than augmented by the addition of electrical stimulation. Many clinicians consequently think that the exact value of electrotherapy in treating peripheral nerve injuries has still to be determined (see Newman *et al.* 1940).

Even among supporters of electrotherapy there is still difference of opinion as to the type of electrical current to be used and as to whether it should be used from the beginning, in the late stages of denervation or after recovery of movement. Moreover many clinicians and experimental workers have only used weak current strength, avoiding any prolonged applications of greater strengths, because of the widely accepted but unproved contention that vigorous contractions and prolonged electrical exercise of denervated muscles may produce additional damage through the excessive fatiguability of denervated muscles.

The experiments which are described in this paper provide further evidences of the beneficial effect of galvanic exercise on denervated and re-innervated muscles. An attempt to find the optimum manner of application, time for starting, duration, and strength of treatment is also described.

Methods

In a series of 30 rabbits the muscles treated were those innervated by the peroneal nerve. No attempt was made to use animals of the same age, weight or family. Therefore it is probable that muscles of different animals atrophied at different rates. However, a control was present in each animal in the opposite untreated muscle so that the results to some extent were rendered independent of this variation. The experiments may be divided into two groups. (*a*) Treatment of denervated muscles without possibility of re-innervation. The peroneal nerve was cut and resected as far as possible on both sides, and the absence of re-innervation of the peripheral stump was confirmed at biopsy. A distinction was made between short-term denervation (37 days) and long-term denervation (67–150 days) and in the second group between early and late start of treatment also. (*b*) Treatment of muscles in which re-innervation was allowed: (1) after crushing the nerve; (2) after division and primary suture of the nerve; (3) after division and secondary suture by cross union. Details of the operative technique will be described later.

Galvanic current only was used in all cases as this type of current is mostly used in man. In all experiments the paralysed muscles of the left leg were exercised while those of the right leg remained untreated. In a single case both sides were treated to compare the effect of different durations of treatment in the same animal. The initial standard method of treatment was 20 minutes galvanic exercise daily at a current strength of 4–6 ma. Copper electrodes of 8 and 3 mm. in diameter covered with gauze and fitted to handles to give a better control were used. Before and during exercise the skin was thoroughly moistened. The anode electrode of 8 mm. diameter was applied at the upper insertion point of the paralysed muscles at the level of the crista tibiæ, but during each daily exercise the point of application was repeatedly altered to avoid local damage to the underlying tissues. The contractions of the muscles were

elicited by the cathode of 3 mm. in diameter, which was applied to the distal part of the muscles. The application of the cathode was not restricted to one position but it was moved along the muscle belly from the proximal to the distal end. The current was thus directed not only longitudinally through the muscles but also to the various parts of the muscle. The contact with the skin was made very light to avoid local damage and to eliminate any effect due to massage of the muscle. With this current strength of 4–6 ma. vigorous contractions of the individual muscles of the peroneal groups could be elicited without giving rise to nociceptive reactions. Since the skin resistance decreases during the electrical exercise the same vigorous contractions can be obtained by progressively weaker current strength. During 20 minutes of treatment about 500–600 single contractions were obtained. In further experiments the effect of this method was compared with others in which current strength and time of application was modified (see Table I).

The following observations were made during the treatment. (*a*) At weekly intervals measurements of the circumference of the leg 15 mm. below the crista tibiæ were made with a fine thread. Three separate measurements were made at each examination and the mean value recorded. Though this method is somewhat crude it proved sensitive enough to give some indication of the difference in volume between treated and untreated muscles. It cannot be expected that this method will give a very exact index of the changes in denervated muscles, especially in young animals where growth processes are taking place. But even in such cases an approximate index of the course of volume changes during denervation and re-innervation of the treated and untreated muscles can be obtained. (*b*) Occasional measurements of the thresholds of the direct excitability of the muscles to faradic current applied through the skin. (*c*) Time of onset of recovery of motor function, using the spreading reflex of the toes. The amplitude of the spreading was determined, to indicate the difference in the degree of the recovered motor function at the end of treatment between treated and untreated side (Gutmann and Guttmann, 1942).

At the end of treatment a biopsy was made under nembutal anæsthesia and the muscles were exposed on both sides. The following observations were then made. (*a*) Macroscopical appearance of the muscles. (*b*) Response of the muscles to stimulation with faradic current. (*c*) The presence and intensity of fibrillation in the denervated muscles, which could be detected easily by reflecting light from the surface of the exposed muscles. Care was taken to avoid cooling which may abolish fibrillation (see Tower, 1939). (*d*) Weight of the extirpated muscles (M. tibialis ant. and M. extensor dig.). The muscles were excised at analogous points from the living animal at biopsy, put in a Petri dish with Ringer-soaked gauze and weighed after blotting twice with filter paper. Although the weight of extirpated muscles is generally considered as the standard measurement of muscular atrophy it cannot be regarded as an absolutely satisfactory index, as it measures both the weight of the contractile muscle substance and that of other constituents of the muscle (e.g. connective tissue).

TABLE I.—EFFECT OF GALVANIC EXERCISE ON MUSCLES ALLOWED TO ATROPHY WITHOUT RE-INNERVATION

Rabbit	Treatment after operation (days)		Duration of daily treatment (minutes)	Current strength (ma.)	Weights of M. tibialis ant. (gm.)		Weight of treated in per cent. of untreated	Circumference of leg (mm.)		Mean diameter of muscle fibres (μ)	
	start	duration			treated	untreated		treated	untreated	treated	untreated
679	7	30	20	5	2·28	1·45	157	85	78	—	—
971	7	30	20	5	1·58	0·89	177	79	75	22	16
992	7	30	20	5	1·54	0·87	177	75	71	26	20
1005	7	30	20	5	2·20	1·56	141	—	—	—	—
892	7	30	10	5	1·97	1·49	132	82	79	24	20
893	7	30	30	5	2·68	1·60	167	73	71	31	23
1017	7	30	20 (twice weekly)	5	1·46	1·36	107	73	70	25	23
983	7	30	20 (twice weekly)	5	0·80	0·66	121	73	71	19	17
981	7	30	15 contractions daily	5	0·86	0·79	109	67	67	22	20
1016	7	30	20	0·5–1	1·47	1·20	122	77	75	23	20
956*	7	30	30 (left) 10 (right)	5	1·95	1·78	109	83	80	26	21
957	7	60	20	5	2·37	1·30	182	79	74	29	20
970	7	90	20	5	2·47	1·53	161	81	73	29	20
895	90	60	20	5	1·07	0·95	113	78	77	18	16
909	90	60	20	5	1·34	1·06	126	79	77	23	19

* Animal in which the left side (see under " treated ") was treated for 30, the right side (see under " untreated ") for 10 minutes.

(*e*) Histological study of the treated and untreated muscles. The muscles were fixed in Bouin's fluid and frozen sections were cut and stained with the van Giesen technique. The atrophy in the treated and untreated muscles was compared quantitatively by finding the mean diameter of a sample of muscle fibres. The measurements were done with a micrometer eye-piece and the samples were taken from the longest diameter of the section, 200 fibres being measured in each muscle. Starting at the edge of the preparation a group of 20 contiguous fibres was measured. The scale of the micrometer eye-piece was then moved on a distance equal to $\frac{1}{10}$ of the diameter of the whole section and 20 more fibres measured and so on across the muscle. This method gives a near approach to a random sampling, though perhaps there is a tendency to omit measurements of very small fibres. It provides a means of measuring representative and corresponding samples of each muscle.

Results

The effect of galvanic exercise on denervated muscles without re-innervation.

1. Short-term denervation

In Table I the first 11 animals are cases with short-term denervation (37 days). In all these animals galvanic exercise started at the 7th day following denervation and was continued for 30 days. In some of these cases current strength and time of daily application of treatment was modified (see later). The 7th day was found suitable for an early start of treatment. During the days immediately after operation the skin over the anterolateral aspect of the leg is often œdematous and easily becomes inflamed. In all cases except those in which the muscles were either treated with weak current strength (animal 1016) or for a short time only (983, 1017, and 981), the beneficial effect of the galvanic exercise was obvious in every respect. The treated muscles kept a good contractile power contrasting with the slow and sluggish contraction of the untreated muscles to direct stimulation. In all cases there was a lower threshold of direct excitability of the muscles on the treated side (see Gutmann and Guttmann, 1942). Of interest was the observation that, during the galvanic exercise a vasodilatation with an increase in the volume of the treated muscles developed 4–7 minutes after beginning of treatment.

At the end of treatment the circumference and weight were found in all cases to be greater in the treated than in the untreated muscles (see Table I). At biopsy the macroscopical appearance of the treated muscles was healthy and hardly differed from that of the normal muscles. In most of the cases the pallor of the untreated muscles contrasted strikingly with the red colour of the treated muscles. Both treated and untreated muscles showed fibrillation. The histological examination revealed less severe atrophy after treatment, the mean diameter of the muscle fibres being in all cases greater in the treated muscles, while the epi-, peri- and endomysium were all thinner in the treated muscles than in the untreated.

2. Long-term denervation

Four animals were left denervated for longer periods (67–150 days). The animals were treated 20 minutes daily with a current strength of 5 ma. to allow comparison of the effect of early and late commencement of treatment. The result is strikingly in favour of early commencement of treatment (see Table I). In two cases (957, 970) the treatment was started 7 days after denervation, the period of denervation being 67 and 97 days. The effect of treatment was very marked in both cases, showing that the treatment is able to retard the rate of atrophy effectively through longer times of denervation. Measurements of circumference enabled us to follow approximately the successive changes in treated and untreated denervated muscles over longer periods (see Fig. 1). It appears from this

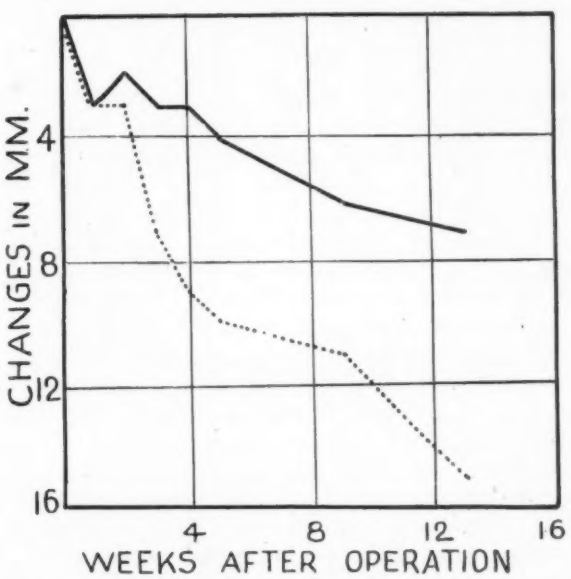
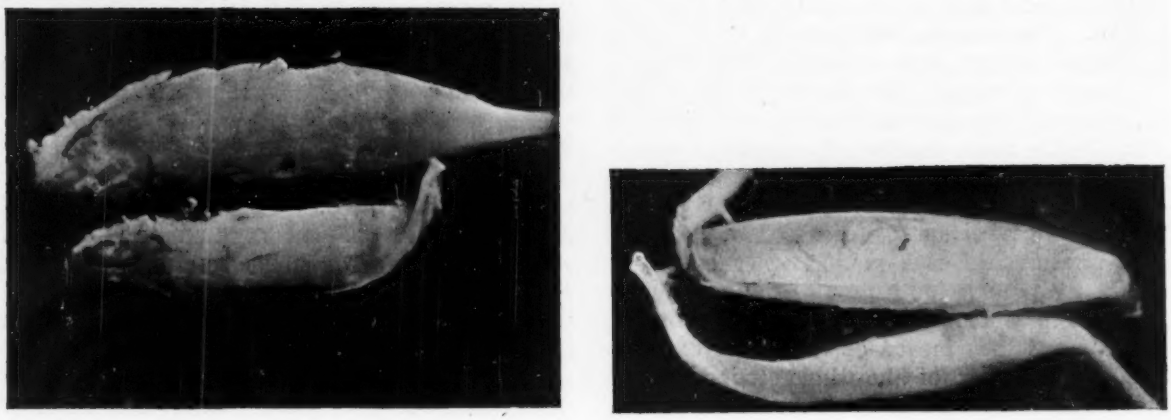


FIG. 1.—Changes in the circumference of the legs, measured by cotton thread, of rabbit 970, in which the peroneal nerve was resected on both sides. Galvanic exercise of the left leg (full line) was begun 7 days after operation and was continued for 90 days.

that the main effect of treatment is achieved in the first month. As the rate of atrophy is quicker during this initial period this is to be expected. In both animals a good contractile power of the denervated muscles was preserved throughout the whole treatment. Clear differences were also revealed by the macroscopical and histological appearance of the exposed muscles (see Figs. 2 and 3). The degree of atrophy was not the same in all parts of the muscle. The effect of treatment was especially marked in the outer parts of the muscle, where there was no increase in connective tissue and where the muscle fibres seemed to have escaped the effect of denervation almost completely.



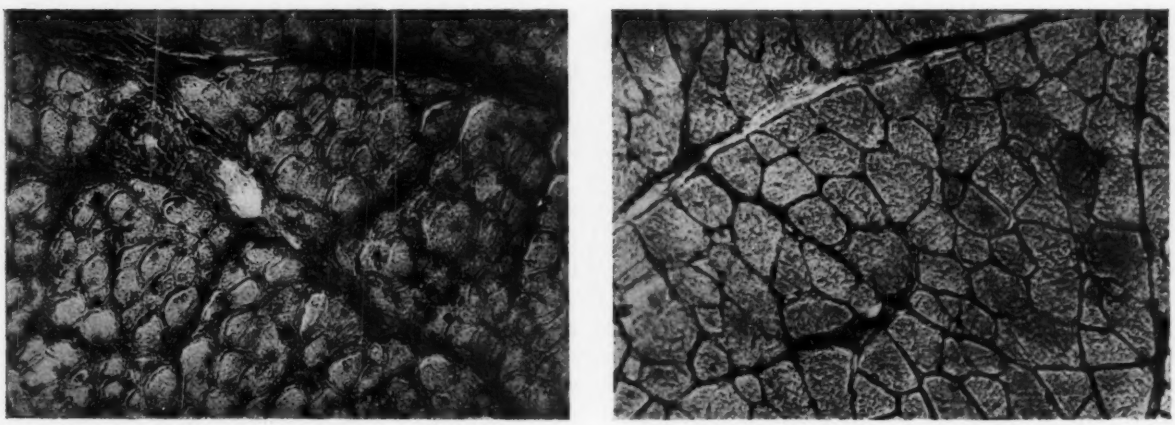
(*a*) (*b*)

FIG. 2.—Tibialis anterior muscles (*a*) and Extensor digitorum muscles (*b*) of the treated and untreated legs of rabbit 957. Galvanic exercise of the left leg was begun 7 days after operation and was continued for 60 days.

In contrast to these two cases the effect of galvanic exercise was definitely less conspicuous in the cases with late start of treatment (895, 909). The treatment was started 90 days after denervation and continued for 60 days. At the beginning the muscles on both sides showed advanced atrophy, their circumferences being square. At first the muscles of the treated side showed the same sluggish and weak responses to galvanic stimulation as those of the untreated side. There was also a considerable fatigue to repeated stimuli, so that after an exercise of 3–5 minutes the muscles ceased to react altogether, and only contractions of the normal muscles of the tibial group were obtained. The treatment was, however, continued daily, the exercise being gradually increased in current strength and duration. After about 10 days an exercise of 20 minutes became possible and the muscle contraction became brisker and there was less sign of fatigue. At the end of treatment the difference in circumference and weight was much less than in the animals with early start of treatment, but the histological examination revealed some difference in favour of the treated muscles (see Fig. 4). The muscles were heavier and the muscle fibres larger and there was less connective tissue on the treated side (see Table I).

3. Evaluation of various modes of treatment (With special reference to minimal and maximal treatment)

As mentioned before, in several cases various modifications of the standard technique were employed (Table I). In animal 981 only 15 contractions were elicited daily. This method had been used by Chor *et al.* (1939). In two other animals the duration of the daily exercise was 10 minutes (892) and 30 minutes (15 minutes twice daily) (893) respectively. The current strength was unchanged. As shown in Table I good results can be obtained by 10 minutes' treatment only, provided sufficient current strength is used to elicit vigorous contractions of the denervated muscles. The results which were obtained in the animals treated for 20 minutes and in that (893) treated for 30 minutes daily did, however, seem better. The superiority of the longer treatment, although not very marked, can be seen in animal 956 in which the left side was treated for 30, and the right side for 10 minutes only. In two animals (983, 1017) a treatment of 20 minutes duration was given twice weekly. This exercise proved ineffective as compared with the daily exercise of 30, 20 or even 10 minutes duration. In a further experiment (1016) the duration of 20



(*a*) (*b*)

FIG. 3.—Cross-sections of untreated (*a*) and treated (*b*) muscles of rabbit 957.

TABLE II.—COMPARISON OF MUSCLES GIVEN MAXIMUM TREATMENT WITH NORMAL AND ATROPHIC MUSCLES

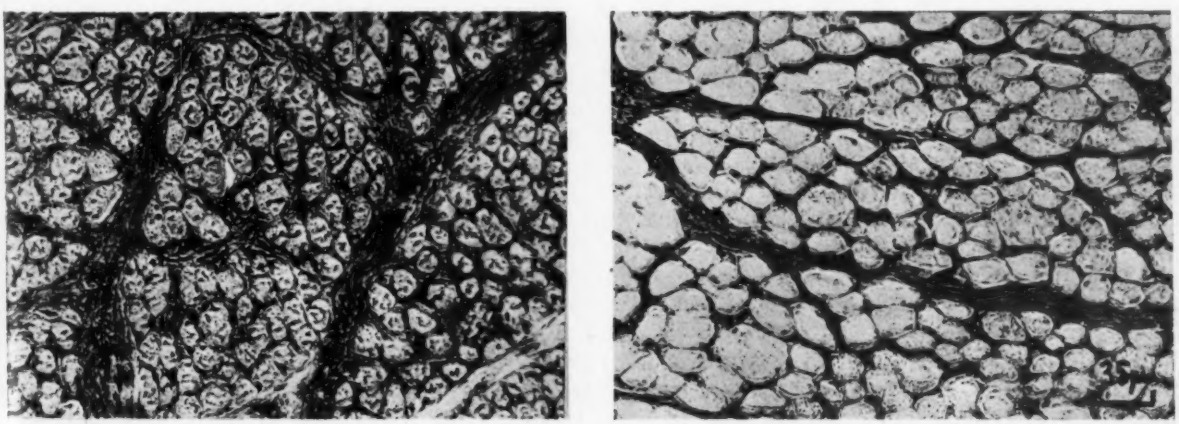
Rabbit	Period of denervation (days)	Weight of M. tibialis ant. (gm.)		Weight of denervated muscle as per cent. of normal	Mean diameter of muscle fibres (μ)	
		normal	denervated		normal	denervated
934 (denervated, treated) ..	60	2·65	2·20	83	38	32
761 (denervated)	60	2·48	1·02	41	36	17
856 (denervated)	60	2·08	0·88	42	36	19

minutes was unchanged but the current strength was reduced to about 1 ma., a current strength which elicited very weak and just visible action of the muscles in the rabbit, the method used by Molander *et al.* (1942). This treatment also had a negligible effect.

Comparison of treated and untreated denervated muscles alone does not allow us to determine to what extent atrophy can be prevented, or particularly whether it can be completely prevented by galvanic exercise. This can only be decided by comparison of treated denervated with the normal muscle of the opposite side. In animal 934 (see Table II) the peroneal nerve was resected on one side only. A maximal treatment lasting for one hour daily (30 minutes twice daily) was started immediately after denervation and was continued for 2 months. No attempt was made to avoid fatiguing of the exercised muscles. As a control the same operation was performed in two further animals but without treating the denervated muscles. As shown in Table II the weight loss of the treated denervated muscle (934) was only 17 per cent. compared with 59 and 58 per cent. weight loss in the denervated untreated muscles (animals 761 and 856). Similar relations are shown when the mean diameters of the muscle fibres in the treated denervated, untreated denervated and normal muscles are compared (see Table II).

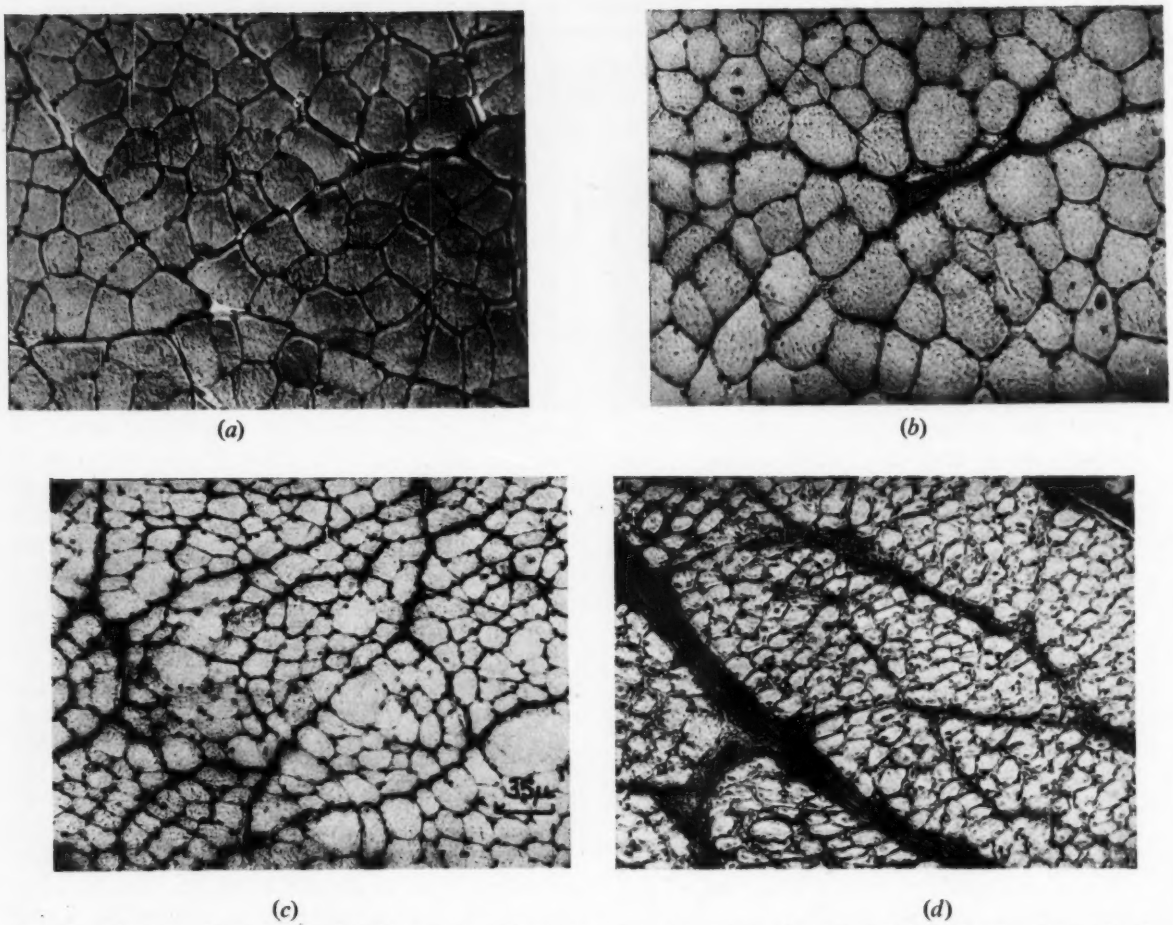
The histological conditions of the muscles of animals 934 and 856 are shown in Fig. 5 *a*, *b*, *c*, and *d*. As already noted the histological picture in a treated denervated muscle is not the same in all parts of the muscle. Differences in the rate of atrophy between different parts of the muscle can be found in untreated denervated muscles, larger muscle fibres being found in the more peripheral parts. The difference is especially marked in denervated treated muscles, and evidently there is a greater effect upon the muscle fibres which lie close to the electrodes. In the maximally treated muscle the outer parts (see Fig. 5*b*) show an almost normal appearance (Fig. 5*a*) but in the inner parts the atrophy has not been so effectively prevented (Fig. 5*c*), but no part of the treated muscle shows the same advanced degree of atrophic changes as the denervated one (see Fig. 5*d*). This observation applied not only to the size of the muscle fibres but particularly to the increase in connective tissue (compare 5*d* and 5*c*).

The differences in fibre size and fibre size distribution of treated denervated, untreated denervated and normal muscles are shown in the histograms of Fig. 6. The upper diagram of Fig. 6*a* relating to animal 934 shows the distribution of fibre diameters in the muscle of the normal side (mean diameter 38μ), the lower that of the maximal treated denervated muscle (mean diameter 32μ). This latter histogram shows the skewed distribution of fibre diameters which seems to be characteristic of denervated muscles.



(*a*) (*b*)

FIG. 4.—Cross-sections of untreated (*a*) and treated (*b*) muscles of rabbit 909. Treatment was begun 3 months after operation and was continued for 60 days.



(*a*) (*b*)

(*c*) (*d*)

FIG. 5.—Cross-sections of M. tibialis anterior (*a*) of the normal control side, (*b*) peripheral part of muscle given maximal treatment, (*c*) central part of muscle given maximal treatment (animal 934), (*d*) untreated muscle denervated for the same time as (*b*) (animal 856) and (*c*).

Fig. 6*b* shows the histogram of animal 856. The upper diagram shows the distribution of the fibre diameters of the normal muscle (mean diameter 36μ), the lower that of the untreated denervated muscle (mean diameter 17μ). Comparing the histograms of animal 934 and 856 it appears that the mean diameter has shifted much more towards the smaller values in the denervated untreated, and that there are more large fibres in the treated denervated muscle. Fig. 6*c* shows the histogram of animal 970 in which the muscles of the left leg were treated for 3 months whereas the denervated muscles of the right side remained untreated. Both histograms show a skewed distribution, but the mean diameter is higher and the histogram has a broader base in the treated denervated muscle, indicating that more muscle fibres of large diameter have been kept intact.

The effect of galvanic exercise on denervated muscles with nerve repair

1. After crushing

In a previous paper it has been shown that after crushing the peroneal nerve with fine watchmaker's forceps, about 80 mm. from the M. peroneus longus, 20 minutes daily treatment with a current strength of about 5 ma. produced no significant difference in the time of onset of motor recovery (Gutmann and Guttmann, 1942). The data from these animals are given in Table III for comparison. The difference in muscle weight was clear in all cases. In animal 390 (see Table III) treatment was continued for 85 days after the first reappearance of motor function. The final differences in weight and circumference between treated and untreated muscles were not great, but where biopsy was performed shortly after motor recovery the differences in muscle weight and circumference (Fig. 7) were found to be much greater.

It appears therefore that the differences between treated and untreated muscles are partly equalized in the months following recovery. Muscles regain their initial weight after crushing about 3 months after recovery, even when no treatment is applied (E. Gutmann, 1942). It must be remembered, however, that crushing at a single point at a relatively short distance from the muscle gives ideal conditions for the re-innervation. Reflex response of the muscle begins after about 40 days and therefore atrophic changes never become severe.

2. After primary suture

After cutting the peroneal nerve in the middle of the thigh the primary or secondary suture was made by the fibrin method of Young and Medawar (1940). In the first 4 cases of primary suture the galvanic

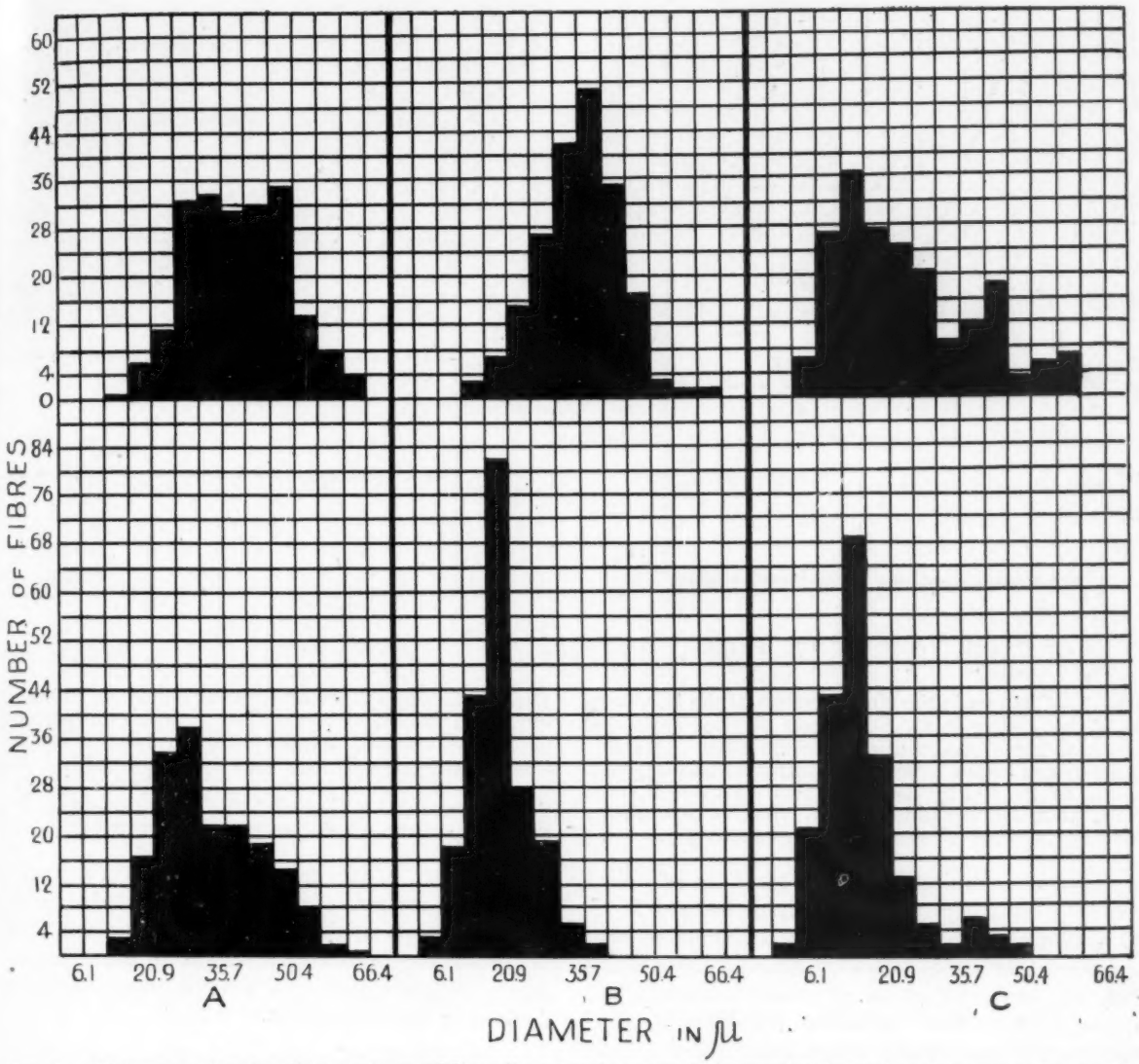


FIG. 6.—Histogram showing the spectrum of fibre diameters in normal, denervated treated and denervated untreated muscles. (*a*) Animal 934—normal (upper diagram) and treated (lower diagram) side. (*b*) Animal 856—normal (upper diagram) and denervated untreated (lower diagram) side. (*c*) Animal 970—treated denervated (upper diagram) and denervated untreated (lower diagram) side. For further details see text.

TABLE III.—EFFECT OF GALVANIC EXERCISE ON MUSCLES ALLOWED TO BECOME RE-INNERVATED

Rabbit	Treatment after operation		Time of recovery (days)		Weights of M. tibialis ant. (gm.)		Weight of treated in per cent. of untreated muscle	Circumference of leg (mm.)	
	start	duration	treated	untreated	treated	untreated		treated	untreated
				After crushing					
390	1	125	48	48	3·72	3·41	109	90	88
588	7	46	39	40	2·40	1·65	145	76	74
536	20	34	41	41	1·35	0·95	142	79	75
623	20	34	41	43	1·94	1·32	147	81	78
				After primary suture					
521	7	87	74	79	3·16	1·92	165	96	91
590	28	35	53	56	2·45	1·44	170	84	78
589	28	96	56	59	2·55	1·95	131	81	74
604	28	96	68	72	2·90	2·30	126	92	83
941	7	60	61	62	3·45	2·90	119	90	86
942	7	60	63	69	1·26	1·10	114	82	79
				After secondary suture (cross union)					
512	7	107	—	—	0·82	0·60	137	68	67
606	7	128	—	—	2·22	0·98	227	67	59
605	67	68	—	—	0·90	0·75	120	59	54

In all cases, except 941 and 942, treatment was continued until biopsy. In these two animals treatment was interrupted at the first appearance of motor function. Biopsy was then performed 4 months later.

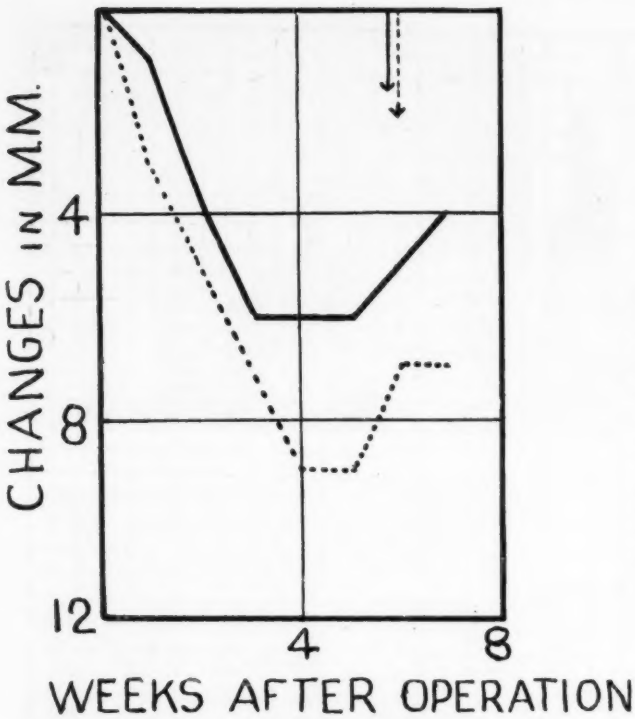


FIG. 7.—Changes in the circumference of the legs, measured by cotton thread, of rabbit 588 in which the peroneal nerve was crushed on both sides. Galvanic exercise was begun 7 days after operation and was continued to the end of the experiment. Treated leg (full line), untreated leg (dotted line). The vertical arrows indicate the times of onset of functional recovery.

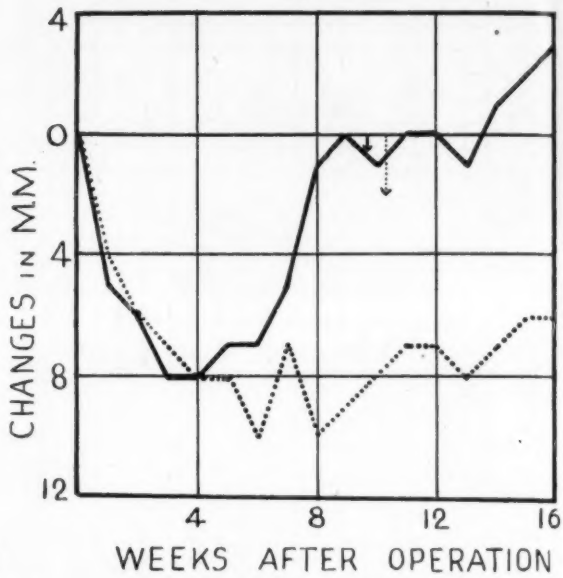


FIG. 8.—Changes in circumference of the legs, measured by cotton thread, of rabbit 604, in which the peroneal nerve was cut and sutured on both sides. Galvanic exercise was begun 28 days after operation and was continued to the end of the experiment. Treated leg (full line), untreated leg (dotted line). The vertical arrows indicate the times of onset of functional recovery.

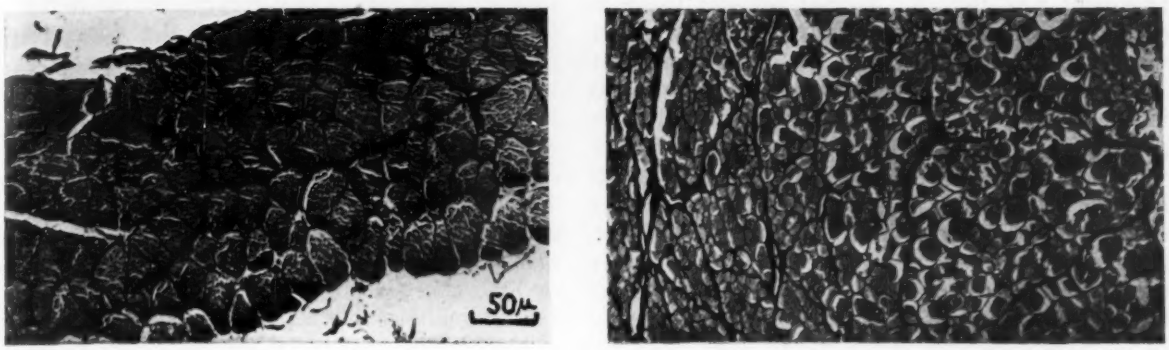
exercise was continued beyond the time of motor recovery until biopsy, which was performed 7, 15, 52, and 65 days after the first reflex movement appeared (see Table III). Comparing the animals 590, 589, and 604, in all of which treatment was started 28 days after operation, the effect of treatment is more conspicuous in animal 590 in which the biopsy was performed 7 days after onset of motor recovery than in animals 589 and 604 in which biopsy was performed at a later date (52 and 65 days after motor recovery). The initial differences resulting from treatment are equalized after recovery, but less completely than in the quick recovery after crushing the nerve. The measurements of circumference in animal 604 show that on the treated side the muscles regain their initial volume much more quickly than on the untreated side (Fig. 8).

Recovery of motor function was observed slightly earlier on the treated side, but the difference was small and probably not significant. But in all cases the spreading of the toes regained greater amplitude on the treated side.

The question arises to what extent the differences in weight are maintained in the treated muscles after interruption of the treatment. In 2 animals (941 and 942) treatment was started 7 days after operation and continued until the time of motor recovery. The treatment was then interrupted and the muscles examined by biopsy 4 months later. The effects of the therapy are certainly equalized to some extent during recovery (see Table III) but clear differences still remain. Histological examination reveals that the muscle fibres are larger on the treated side, the mean diameter of the muscle fibres in animal 942 being 35μ on the treated and 30μ on the untreated side. Moreover there is less connective tissue in the muscles of the treated side.

3. After secondary suture by cross union

To obtain longer times of denervation secondary sutures by cross unions have been used. This method allows delayed suturing of a nerve but has the disadvantage of producing defective function and of the difficulty in estimating the onset and degree of motor recovery exactly. It is, therefore, difficult to estimate the degree to which muscles have recovered after re-innervation, but the experiments provide further evidence of the effect of therapy on muscles which have been re-innervated after prolonged periods of denervation. At an initial operation the peroneal nerve was cut and resected on both sides. Two months later a second operation was performed in which the tibial as central stump was sutured into the peripheral stump of the peroneal nerve. Treatment of the left side started either 7 days after the first (animal 606) or second operation (animal 605) and was continued about 2 months after the second operation, at which time a biopsy was performed. It can be seen that the differences in weight and circumference are definitely more conspicuous in the case 606 in which treatment



(*a*) (*b*)

FIG. 9.—Cross-section of treated (*a*) and untreated (*b*) muscles of rabbit 606, in which the peroneal nerve was resected at an initial operation and sutured with the tibial as central stump at a second operation 2 months later. Galvanic exercise of the left leg (full line) began 7 days after the first operation and was continued to the end of the experiment.

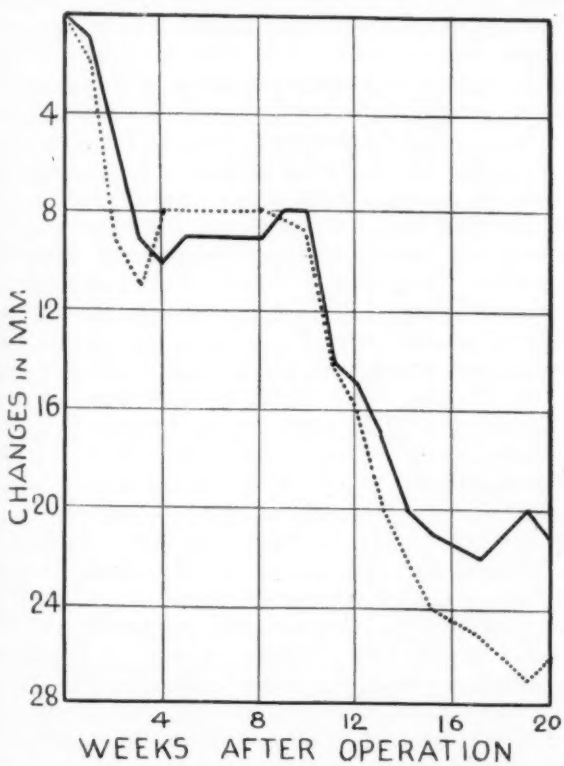


FIG. 10.—Changes in the circumference of the legs, measured by cotton thread, of rabbit 605, in which the peroneal nerve was resected at an initial operation and sutured with the tibial as central stump at a second operation 2 months later. Galvanic exercise of the left leg (full line) began 7 days after the second operation and was continued to the end of the experiment.

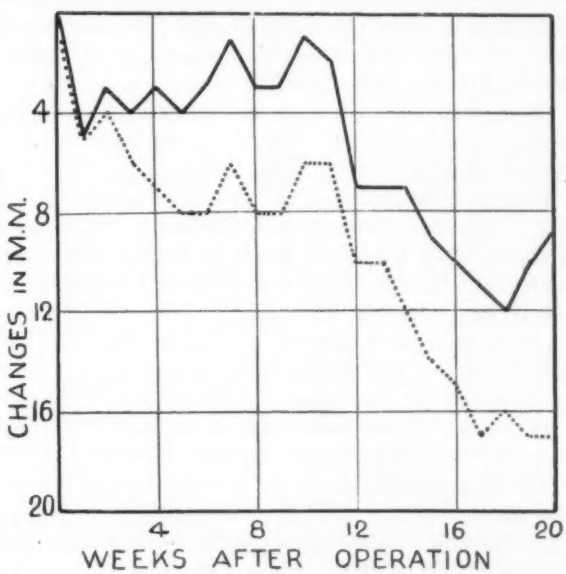


FIG. 11.—Changes in the circumference of legs, measured by cotton thread, of rabbit 606, in which the peroneal nerve was resected at an initial operation and sutured with the tibial as central stump 2 months later. Galvanic exercise of the left leg (full line) began 7 days after the first operation and was continued to the end of the experiment.

was continued throughout the whole period of denervation.

Fig. 9 shows a cross-section of the treated and untreated muscle in animal 606. The muscle fibres are larger and there is less connective tissue on the treated side. Figs. 10 and 11 show the results of measurement of the circumferences in animal 605 and 606. In animal 606 the degree of atrophy is considerably less, while recovery of muscle volume proceeds more quickly after re-innervation.

Animal 512 of the same series is of special interest for treatment was also started on it 7 days after the first operation. After the second operation in which the cross union was performed the animal fell ill and lost heavily in weight, became extremely emaciated and died two weeks before the planned treatment was finished. As shown in Table III the effect of treatment was much less marked compared with animal 606 in which the identical experiment was made. The poor general state of the animal 512 was apparently the reason for the relatively slight effect of the galvanic exercise.

Discussion

The results of all these experiments show clearly that the effect of galvanic exercise varies with its time and duration of application. The effect in preventing atrophy was found to be especially marked after daily application, with a current strength sufficient to elicit vigorous contractions of the muscles. The effect was greater the earlier the

treatment was started. Twenty minutes galvanic exercise gave very satisfactory results and has been used as the standard time of application, but 10 minutes daily exercise gave results only slightly inferior, while 30 minutes exercise showed little superiority to 20 minutes. No damage of denervated muscles was detected by the longer duration of daily treatment. It may be remembered that even in animal 934 in which no attempt was made to avoid fatiguing the denervated muscles a very satisfactory result was obtained. These findings, which agree with those of Fischer (1939) and Hines, *et al.* (1943) do not support the view held by many physiologists and clinicians that galvanic exercise of paralysed muscles should not be used during the period of denervation, especially in the early stages. In fact no harmful effect of fatigue on denervated muscles of the rabbit was found and the results indicate that fatigue of denervated muscles by galvanic exercise in man may not be so harmful as formerly thought.

The main effect of treatment was seen during the period of denervation. But even when the muscles were followed into the later stages of recovery the differences between treated and untreated muscles were still clear, though less marked. The treated muscles were found to be in a better state even 4 months after the galvanic exercise had been discontinued (animals 941 and 942).

After re-innervation of a muscle its " trophic state " will be restored spontaneously to a greater or less degree by voluntary impulses. Although there cannot be any doubt that in man active exercise by voluntary impulses is the best treatment for a recovering muscle, it must be remembered that at the time of motor recovery muscle atrophy is still very marked and the power of voluntary or reflex movement is limited. Moreover, longer times of denervation and less successful re-innervation can be expected in most of the human cases. It is, therefore, advisable to continue electrical exercise until motor recovery is satisfactory, for as clinical experience has shown electrotherapy is most useful in augmenting active exercise in cases in which the patient co-operates poorly although re-innervation of the muscles is taking place (Guttmann L., 1942).

It is still an unsettled question whether during the periods of denervation and re-innervation other forms of electrical current (sinusoidal, faradic) may be preferable to galvanic current in man as well as in animals. It must be remembered that in most human cases re-innervated as well as denervated muscles do not respond to faradic stimuli at the beginning of functional recovery, so that any treatment with faradism of such muscles is useless. Recently Solandt *et al.* (1943) found in rats that a sinusoidal current of low frequency (25 cycles) was more effective than other forms (galvanic, faradic and sinusoidal current of 60 cycles). These interesting experiments were concerned only with the first period of denervation (11 days treatment after denervation) and it still remains to be seen whether the treatment employed will prove more effective in the later stages of denervation and during early stages of recovery, and whether the current used will cause less irritation of sensory fibres and so be better tolerated. These authors also found that the effectiveness increases with the number of treatments daily but that no differences are obtained by varying the length of treatment within the limits employed (1–5 minutes). In the present experiments, however, it was found that treatment had no or little effect when applied for a short time only (15 contractions daily).

The demonstration of the beneficial effect of galvanic exercise on denervated muscles has an important bearing on the problem of the cause of denervation atrophy which is still the subject of controversy. The theory of Langley and Kato (1915) that atrophy of denervated muscles is a fatigue phenomenon caused by ceaseless fibrillation was widely accepted until quite recently (Tower, 1937). The negative experimental results of Langley and Kato on electrotherapy and their statement that " the fact that the denervated muscles are in a state of continuous fibrillation makes it *a priori* an open question whether further activity caused by electrical stimulation will be beneficial " seems to have influenced many clinicians to condemn galvanic exercise. In spite of the beneficial effect of galvanic exercise described in the present experiments all the treated muscles were found to be still fibrillating, even those given maximum treatment and showing little atrophy. No significant difference in the intensity of fibrillation between treated and untreated muscles was observed at visual inspection. Fibrillation definitely follows denervation but there is no proof that it is the immediate cause of atrophy. In recent years this problem has been repeatedly discussed and although it is still unsettled some results suggest a relative independence of atrophy and fibrillation. Solandt and Magladery (1940) found in rats that quinidin reduces or abolishes fibrillation without greatly affecting atrophy. Weddell, *et al.* (1943) found no correlation in electromyographic studies between the degree of fibrillation and the rapidity of muscle atrophy.

Most of the negative results of electrotherapy have been due to inadequate technique. The effect of the condensor discharges used by Langley and Kato (1915) was very small and they stated " either then the daily induced contractions were insufficient in number to replace the normal contractions or the change in the muscles is not simply an inactivity atrophy." In fact, comparison of intensive with insufficient treatment, described here, indicates that the first explanation of Langley and Kato is the correct one (see also Fischer, 1943). Such findings also explain the negative results described in recent years by Chor *et al.* (1939) and Molander *et al.* (1941.) Moreover, these authors and others (Hartmann and Blatz, 1920) combined inadequate technique with skeletal immobilization of the paralysed limbs, a method which in itself can produce atrophy (Solandt, 1942) or retard the recovery of

muscle volume and strength after re-innervation (Hines, 1942).

The experiments described here reveal the great importance of activity as the leading factor in preventing muscular atrophy. Although the present experiments (see case 934) do not prove that inactivity is the only cause of atrophy after denervation, they show clearly that the impulses which are responsible for the normal muscular activity and which are lost after denervation can be effectively replaced by galvanic exercise.

Activity appears to be the important factor for the healthy " trophic state " of a muscle. Recently Hines *et al.* (1943) found in denervated muscles a greater creatine content on the side which was treated with induction shocks. It appears that galvanic exercise produces better metabolic conditions for the denervated muscle. How these better metabolic conditions are achieved is still unknown, but the effect of exercise on the circulation may possibly be responsible. This is suggested by the development of vasodilatation and increase of volume observed after onset of treatment. In fact muscle activity increases the circulation, and the volume of blood in an active muscle may be 3–5 times that found in an inactive one (see Mann, 1936). It is notable that electrotherapy has been found to be less effective in human subjects in whom there has been damage to the vessels in addition to the nerve lesion, either at the time of injury or as the result of later plaster or splintage (Guttmann L., 1942).

It might be thought that the increased metabolism, which prevents atrophy in denervated muscles, is due mainly or entirely to the ionic (cataphoretic or electro osmotic) or thermal effects of the current, but methods such as heat, diathermy, short waves and uninterrupted galvanic current have so far proved definitely inferior to interrupted galvanic current in preventing atrophy of denervated muscles. Moreover, the experiments described here show that interrupted galvanic current failed to prevent atrophy if it produced only feeble contractions, while vigorous contractions produced by daily galvanic exercise go far towards replacing the reflex and voluntary impulses which normally maintain the action of the muscle and its normal metabolic conditions.

Summary

Daily application of galvanic exercise with a current strength sufficient to elicit vigorous contractions of the muscles was found to delay and diminish atrophy in denervated and re-innervated rabbit muscle. The most satisfactory results were obtained with a daily exercise of 20–30 minutes duration. The effect was greater the earlier the treatment was started following denervation.

Treated muscles showed larger muscle fibres and less fibrosis than untreated ones.

After a maximal treatment (1 hour daily), beginning immediately after denervation, the muscles lost only 17 per cent. in weight in 60 days, compared with a loss of 59 per cent. in untreated muscles.

No attempt was made to avoid fatiguing of the stimulated muscles during the exercise and this did not prevent the beneficial end effect.

The main effect of the treatment appeared during the period of denervation but a difference was still demonstrable 4 months after interruption of the galvanic exercise. The effect of treatment is therefore not masked by the normal process of muscle recovery after re-innervation.

No certain effect of galvanic exercise was found on the time of onset of motor recovery, but the degree of motor recovery was higher in the treated muscles.

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MYELITIS DUE TO VACCINATION

BY

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(RECEIVED 27TH OCTOBER, 1943)

MYELITIS as part of a post vaccinial encephalomyelitis is well known, and histological changes occurring in the spinal cord were fully described in the earlier case records (Turnbull and McIntosh, 1926). The purpose of the present paper is to draw attention to the fact that myelitis uncomplicated by encephalitis also occurs as a sequel to vaccination. The following case which I have recently had the opportunity of observing is typical of this group.

An R.A.F. recruit, aged 27, received his primary vaccination 3rd September, 1942, over the left deltoid, and at the same time received an injection of 0·25 c.c. of T.A.B. and 1 cc. of A.T.T. vaccines in the right arm. On the 12th he received a second injection of 0·5 c.c. of T.A.B. He sweated that night and felt feverish, suffered from stabbing pains in the arms, especially at site of vaccination: the pains persisted for some days. As they passed off he developed pain in his calves and feet, and noticed that his legs were not properly under control. He did not report sick till the tenth day of his illness when he fell on parade. He was admitted to Station Sick Quarters, where he was found to be feverish. The fever continued for four or five days, pain and weakness of his legs was more persistent, but a full neurological examination soon after admission to Sick Quarters is reported to have revealed no objective signs. He was discharged from Sick Quarters after seventeen days illness and did light duty for five days, then on the 5th of October, on getting out of bed, he found that his legs were stiff and wobbly and he had no control of his bladder. The condition appears to have been progressive, incontinence becoming complete the next day, and by the twenty-third day of his illness he was completely paralysed from the waist down, with complete sensory loss to the costal margin, absent tendon jerks and plantar withdrawal responses. A lumbar puncture on this day showed a pressure of 170 mm. of fluid, a pleocytosis of 1,500 lymphocytes per cubic mm. and protein 80 mgm. per cent. Five days later it was noticed that the anæsthesia was receding and in another five days some voluntary movement had returned to the toes. Three deep bedsores and urinary infection had unfortunately developed.

Cutaneous sensation was almost completely restored by the 45th day. By January, 1943, approximately 15 weeks after first symptoms, there was sufficient power in all muscular groups to allow movement against gravity at all joints, but the legs were not sufficiently strong to support the patient. The paralysed muscles were now flaccid, the tendon jerks were just obtainable, the plantars were extensor and control of the sphincters had been regained.

Motor power continued to return and he was taught to walk, first supported under the armpits by a machine and later with two sticks in his hands.

In June, 1943 the bedsores were almost completely healed and the patient could, with one stick, walk up to two miles.

On examination there was very little demonstrable muscular weakness, no abnormality of tendon jerks, tone or sensation, though the plantars remained extensor.

The case here described resembles the original 47 cases of post vaccinial encephalitis selected by the Andrews Committee (Vacc., 1928) in being febrile and in occurring within the 2nd to 24th day after vaccination; like the majority, the vaccination was the primary one and like five of the said group, the illness occurred on the 9th day after vaccination; and resembles the majority of the non-fatal cases in the completeness of its recovery.

The increase of protein and leucocytosis are also common features in post vaccinial encephalomyelitis (Vac., 1930). It differs, however, markedly from the 47 classical cases, in that the symptoms were spinal rather than cerebral and there was no headache, vomiting, strabismus or clouding of consciousness.

An almost identical case is described by Gounelle (1931) (see Table). This case, also a young soldier, had a partial remission, and paraplegia developed suddenly on the 13th day of his illness. Such a remission in the course of post-vaccinial encephalomyelitis is not an unusual finding and is in fact described in the first published case (Comby, 1907).

I have been able to trace twelve other cases of myelitis following vaccination within the 3rd to 15th day.

Two of these occurred among the original 63 cases considered by the Andrews Committee (May, 1925) and a further 2 among the 44 cases submitted following Committee's request for further information in the medical press April, 1926. At the time of the publication of the Ministry of Health report on vaccination 1928, these cases of uncomplicated myelitis were not thought to be due to vaccination. In a further report, November, 1930, the Committee describe 3 cases of uncomplicated myelitis among 90 cases of post-vaccinial encephalomyelitis. One of this group is of especial interest as the patient (see Table, 1930, "case 148") died of urinary infection on the 94th day and at autopsy the histology of the nervous system was described "In the pons and spinal cord there are perivascular and marginal areas of demyelination such as are found in post vaccinial encephalomyelitis. The lesions have reached the stage at which fat-granule cells are very abundant (M.M.T.)."

TABULATED FINDINGS OF PREVIOUSLY PUBLISHED CASES OF MYELITIS FOLLOWING VACCINATION

Date and Author	Patient	Incubation	Onset	Physical signs	Progress and result
1943	Male, aged 27	9th or 10th day after primary vaccination	Pyrexia, muscular pains, unsteadiness of legs for 17 days. Partial remission; 23rd day sudden paraplegia and incontinence.	Flaccid paralysis of legs and analgesia below seg. D.5. C.S.F. 25th day protein 0·08 per cent.; 1,500 lymphocytes per c.mm.	Gradual recession of level of anæsthesia, sensation normal in 45 days. Return of motor power in 5 months; persistent extensor plantars.
1942 Anderson and McKenzie, Case 7	Male, aged 16	14th day after primary vaccination	Retension of urine and signs of transverse myelitis in thoracic region.	—	Recovered.
1937 Clouston and Quins	Female, aged 9	5th day after vaccination	Fever and pain in neck for 2 days, weakness of legs, retention of urine. 3rd day paralysis of legs.	Flaccid paralysis and sensory loss below seg. 6 D. C.S.F. on 4th day 5 lymphocytes. No globulin.	Gradual recession of level of anæsthesia starting on 5th day. Gradual return of motor power, in 5 months normal except for exaggerated reflexes.
1932 Paulian, Aricesco and Finkelstein	Female, aged 7	3rd day after 1st re-vaccination	3 days fever two days after vaccination. Two weeks later pains in calves, unable to walk. Retention of urine. Attitude of flexion.	After an interval of less than 6 months spastic palsy in flexion of arms and legs with muscular wasting and no sensory changes.	Recovered power of walking during a 1-month period of observation though obvious quadraplegia persisted.
1931 Gounelle	Male, aged 21	14th day after 1st vaccination	7 days' fever, unsteadiness of legs. Positive Rhomberg's signs and brisk knee and ankle jerks. Partial recovery; 13th day sudden paraplegia and retention of urine.	No notes on sensory findings or exact level of palsy. C.S.F. on 5th day protein 0·056 per cent. 25 lymphocytes per c.mm. Muscular fib. observed in acute phase.	Rapid recovery in one month. Able to return to work.
1931 Brockbank	Male, aged 6	14th day after vaccination	One week's fever with sudden paralysis of legs and retention of urine, anæsthesia to below seg. 7 D. on 2nd day. Spread of anæsthesia to seg. 3 D.	Flaccid paraplegia and doubtful weakness of left arm and anæsthesia. C.S.F. on date unknown pressure 160 mm. 50 cells per c.mm. and Globulin ++	Gradual recession of level of anæsthesia. No further recovery in subsequent 6 months.
1929 Peake	Female, aged 8	8th day after revaccination	Fever and pains in abdomen. 4th day became drowsy and had retention of urine. 7th day paraplegia discovered.	7th day flaccid paraplegia and anæsthesia to umbilical level. Fever persisted about 3 weeks due to urinary infection.	Gradual recession of level of anæsthesia. Sensation normal 50th day, able to walk with slight support on both sides and partial recovery of sphincters in 3 months. * Complete recovery in 6 months.
1930 Further report of Committee on Vaccination, Case 148	Female, aged 46	13th day after revaccination	Fever and pricking sensation in legs; 3rd day motor and sensory paraplegia and disturbance of sphincters.	Flaccid paraplegia to level of higher thoracic segments. Histology, see text.	Death from urinary infection on 94th day. Some evidence of returning of functions of cord as sphincter control was regained before death. Autopsy.

* Personal communication.

TABLE I—*continued*

Date and Author	Patient	Incubation	Onset	Physical signs	Progress and result
1930 Further report of Committee on Vaccination, Case 85	Female, aged 19	10th day after primary vaccination	Headache, vomiting, loss of power in legs and retention of urine.	Considered doubtful. Hysteria suggested as diagnosis.	Uneventful recovery in 18 days.
1930 Further report of Committee on Vaccination, Case 90	Female, aged 12	8th day after primary vaccination	" Transient Myelitis "	—	Recovery after 20 days.
1928 Further report of Committee on Vaccination, Case 10	Female, aged 3 months	15th day after primary vaccination	On or about 10/2/26 developed paresis of both legs.	Positive W.R. in child's and mother's blood. Father's blood negative.	—
1928 Further report of Committee on Vaccination, Case 28	Female, aged 15	7th day after vaccination	Headache and pains in all four limbs. 3rd day rigor, delirium. High fever. Lost use of all 4 limbs.	13th day spastic paresis of arms. Flaccid paresis of legs. Retention of urine. No sensory changes.	Progressive motor recovery. Intermittent fever and persistent bed sores. Death 118th day.
1925 Andrew's Committee, Case 5	Female, aged 13	11th day after vaccination	Pain in back, headache, vomiting, rash and paraplegia.	—	Death on 164th day.
1925 Andrew's Committee, Case 42	Male, aged 20	12th day after vaccination	Retention of urine, girdle pain in upper dorsal region. Paresis and loss of sensation below.	Babinski's sign and knee jerks.	Died.

The details of the other two are scanty, probably because they recovered; doubt is thrown on the diagnosis of at least one.

Six other cases have been published by different authors all of which (see Table) have a close similarity to the case here described.

It is, of course, open to argument that the case here described was caused like that of Gayle and Bowen (1933) by typhoid inoculation, but as these authors point out " such complications are certainly rare " and the disease in the cases they review takes the form of a peripheral neuritis, which sometimes extends into the spinal cord and medulla.

Summary

A case of a young man developing fever, muscular pains and unsteadiness of gait 9 days after primary vaccination, followed by a temporary remission and then a sudden paraplegia on the 23rd day is described. During the subsequent 6 months the patient almost completely recovered. The histories of 13 previously published cases of transverse myelitis occurring between the 3rd and 15th day after vaccination are summarized. Cerebral symptoms indicative of an accompanying encephalitis only occurred in the acute phase of 3 of these cases and even then were overshadowed by the symptoms related to disease in the spinal cord.

I wish to express my thanks to Dr. Fergus R. Ferguson for his help and advice in treatment of this case and to Dr. Joseph Doupe for his help with this paper.

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THE PHYSICAL EXAMINATION OF TWO THOUSAND CASES OF NEUROSIS

BY

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THE material of this paper consists of 2,288 consecutive admissions to a military hospital for neurosis. Selection has taken place before arrival, because only those cases which are considered to have a good chance of rehabilitation are recommended. Age ranges between 18 and 49 with a maximum number at the age of 23. Length of service ranges between 6 weeks and 17 years, with a preponderance at 2½ to 3 years. Only a few old soldiers with 10 or more years service appear in the series.

The proportion of N.C.Os. to other ranks are: Sergeants, Corporals, Lance-Corporals, Privates, in the ratio of 2, 2, 1, 11.

Organic Disease

Of the 2,288 cases, 78 (or 3·4 per cent.) were thought to be suffering from organic disease as the basis of their symptoms.

They were as follows:—

Epilepsy	15
Asthma and Bronchitis	8
Arthritis of Spine	7
Hypertension with early renal involvement	7
Narcolepsy	6
Syphilis	6
Gonorrhœa	5
Meningitic sequelæ	4
Sacroiliac Arthritis	3
Anterior Poliomyelitis	2
Cerebro-spinal Meningitis	2
Duodenal Ulcer	2
Pulmonary Phthisis	2
Sub-clinical malaria	2
Addison's Anæmia	1
Cerebral Neoplasm	1
Diabetes Insipidus	1
Mitral Stenosis	1
Neoplasm Stomach	1
Paroxysmal Tachycardia with early Coronary Disease	1
Spondylolisthesis	1
TOTAL	78

The list is a reminder that many diseases are mistaken in the first instance for neurosis and can only with difficulty be distinguished after investigation. Almost all predominant or common neurotic symptoms are also symptoms of organic disease. For instance, the 7 cases of hypertension all presented themselves as cases of headache, and were separated from a large collection of anxiety headaches. The spinal conditions likewise were weeded out from a very large number of " backaches." One of the cases of anterior poliomyelitis (onset 6 weeks previously and happily mild) was sent in as an hysterical paralysis of the leg ; one of the cases of meningitis arrived in a confused state under escort, with a diagnosis of hysterical amnesia; the case of diabetes insipidus was admitted as a diurnal enuresis.

In addition to the instances in which an established disease was present, a variety of lesser organic conditions were found which contributed to the production of symptoms. Sepsis was prevalent, especially of the accessory nasal sinuses (6 per cent. of all cases), and dental sepsis (4½ per cent. of all cases); an abundance of minor disabilities was present in the shape of pes planus, pes cavus, varicocoele, varicose veins, hernia, boils, errors of refraction, nævus, mole, deviated nasal septum, alopecia, seborrhœic manifestations, psoriasis, etc. In all, 35 per cent. of cases showed some contributory or minor ailment.

Neurosis

The remaining cases were those in which the organic element was minimal. They numbered 2,210. They may be grouped in the following way:—

Anxiety State	464
Dyspepsia	424
Effort Syndrome	313
Rheumatism	228
Hysteria	150
Headache	122
Post Concussion Neurosis	108
Enuresis	71
Fugue	68
Stammer	60
Syncopal Attacks	59
Homosexualism	38
Psychosis	22
Sleep Walking	20
Night Blindness	17
Tic	15
Obsessive Compulsive Neurosis	10
Pruritus	10
Constipation	8
Overbreathing Tetany	1
Alcohol Addiction	1

This is not a psychiatrist's classification. It is a rough grouping according to the most prominent symptoms complained of by the patient.

Those psychosomatic cases in which there appeared to be a definite somatic location for psychogenic symptoms, effort syndrome, dyspepsia, anxiety headache and rheumatism, are the main consideration in this paper. They appear to form a definite group by reason of their somatic symptoms, yet reference to the psychiatric diagnoses in these cases shows that they consist of precisely the same mixture of conditions as the other groups—namely, anxiety neurosis, psychopathic personality, emotional instability, and hysteria.

Blood Pressure

Our conception of " normal " blood pressure is founded upon certain classical studies of large numbers of subjects (Symonds, 1923; Janeway, 1913; Alvarez, 1923; Robinson and Brucer, 1939) which established the belief that a systolic pressure as high as 150 mm. Hg. is to be regarded as abnormal at all ages, and a diastolic of 100 as probably always pathological.

It is well known that blood pressure varies considerably with emotion. The systolic blood pressure may vary as much as 50 mm. Hg. under the influence of emotion and isolated readings of 160 and 170 are not uncommon (Fahrenkamp, 1931, and Mohr, 1925). Hence it is to be expected that neurotics, whose emotional apparatus may be particularly sensitive, would show more frequent and greater variations than normal. This is the case; and our conception of what is a normal blood pressure reading is considerably modified thereby.

Of the total 2,210, 1,901 (86 per cent.) had systolic pressures of 140 or less and diastolics of 90 or less. This leaves 309 (or 14 per cent.) who had systolic or diastolic pressures greater than 140/90. The figures noted were sometimes very much larger, and varied between 140 to 190 systolic, and 90 to 120 diastolic. Those cases in which the readings were unusually high were re-examined after ten minutes rest, or longer, on the couch. Usually a lower figure was recorded. If it was not, the patient was re-examined the next day in the same manner.

With the exception of 7 cases it was possible in every instance to obtain diastolic readings below 100, whilst the systolic fell to a more normal level, usually, though not always, to 140 or less.

Three groups thus separate themselves:—

1. 1,901 patients with habitual systolic and diastolic pressures of 140/90 or less.
2. 302 with systolic and diastolic pressures greater than 140/90, in whom rest and confidence reduced the diastolic to below 100 and the systolic to a lower level than at first.
3. 7 cases in which rest and confidence, though producing some lowering, never reduced the diastolic reading to below 100.

100 cases from Group 1; 150 cases from Group 2; and all 7 cases from Group 3 were investigated by:—

1. Retinoscopy.
2. Urine analysis and microscopy of centrifuged deposit.
3. Concentration and dilution test, judged by specific gravity after fasting or drinking.
4. Urea clearance.

All 7 cases in group 3 gave abnormal findings (Table I). In none of the other cases was abnormality found.

TABLE I.—GROUP III (7 CASES)

Retinal arteries	Casts	Maximum urinary sp. gr. after 12 hours fluid fast	Sp. gr. maximum after 1,500 c.c. water	Urea clearance per cent.	B.P.
N.	—	1,015	1,005	Cs 52	150/110
N.	—	1,019	1,002	Cm 48	165/105
N.	—	1,017	1,008	Cs 42	170/110
N.	—	1,019	1,008	Cs 56	160/105
Marked silver wire	—	1,013	1,010	Cs 48	180/110
N.	—	1,020	1,005	Cm 58	170/110
N.	—	1,019	1,003	Cs 58	170/110

From this it may be concluded that a systolic blood pressure reading up to almost 200 mm. Hg. may be within normal limits, provided the level is not constantly maintained and provided that the diastolic reading is not in excess of 100. A diastolic reading which exceeds 100 is almost certainly pathological.

Further, it has been found almost impossible to judge from the patient's behaviour whether or not his blood pressure reading will depart from usual levels. Before estimating the blood pressure every patient was given an arbitrary rating from 1 to 4 according to whether he appeared calm and undisturbed or showed objective signs of anxiety (such as restlessness, depressed and unhappy facies, twitching, tremor, excessive sweating, pallor, dry disorderly hair, irritability). Table II shows that these four

TABLE II

(All blood pressure readings represent systolic level at orginal interview.)

	1. Systolic 140 or less	2. 140–150	3. 150–160	4. 160–170	5. 170–180	6. 180–190	Totals
1. Normals	592	51	12	12	6	4	677
2.	391	23	25	16	5	5	465
3.	317	41	17	11	5	5	395
4. Most anxious	601	27	20	10	6	2	666
Totals	1,901	142	74	49	22	15	2,203

groups are distributed amongst the different blood pressure levels.

Thus, although the number of patients with high blood pressure readings is smaller than that with low ones, the number of objectively anxious patients with high readings is not, as might be expected, greater than those normals who show high readings (vertical column 6); the number of normals showing normal readings is about the same as that of anxious patients (vertical column 1). Normals and nervous patients are distributed throughout the whole blood pressure scale (vertical column 7). There is, therefore, no relation between blood pressure height and objectively recognizable anxiety.

Exercise Tolerance Test

Unreliability in the cardiac exercise tolerance test has been noted amongst cases of effort syndrome. One hundred and fifty men who showed the typical symptoms of effort syndrome (cardiac discomfort on exertion, breathlessness, dizziness, sweating, tremor, etc., etc.) were examined. In every case physical findings were normal, blood pressure was within normal limits, cardiograph tracing normal, Hb. over 85 per cent. Twenty-nine of these patients showed a deceleration rate in excess of 3 minutes after the standard exercise of mounting a chair 12 times. They were then placed in a physical training class and given very light physical training with no jumping, vaulting, parallel-bar work or running. Most of the exercises were carried out sitting or lying down. After an interval of two days in this class their exercise tolerance was again tested, by running once round the gymnasium. In every case a normal exercise tolerance was recorded.

The improvement in tolerance cannot have resulted from any work done in the gymnasium, because the time was insufficient, nor was the type of exercise carried out likely to lead to any improvement. These men had all appeared nervous during the first examination. It would, therefore, seem that when the patient had had time to settle down and was in a more carefree atmosphere, any nervous factors that may have prolonged the tachycardia after exertion were not operating.

This group was compared with one hundred and fifty physically fit men going through a " Hardening Course," whose neurosis had never consisted of symptoms of effort syndrome, but of enuresis, constipation, pruritus, etc., which had no relation to exertion. In hospital they were occupied on physical training or strenuous physical exertion all day. This group had likewise been tested on admission to hospital, and afterwards in the gymnasium. In no case was a deceleration time noted in excess of two minutes.

Pulse rate, cardiac output, blood pressure, etc., are well known to be markedly affected by psychic stimuli (Braun, 1932; Fahrenkamp, 1931; Grollman, 1932). Deceleration times in excess of two minutes in cases of effort syndrome have been noted by Friedlander and Freyhoff, 1918, and by Wood, 1941. Meakins and Wilson, 1918, have shown that persons in whom sudden emotion causes unusual acceleration of pulse rate when resting have a poor effort tolerance. The discrepancies in effort tolerance test noted here may reasonably be supposed to result from emotional factors, though whether the original abnormal finding was, in fact, due to emotion is not certain.

The Problem of Somatic Location

Great interest centres around the question, " What factors influence the somatic location of psychogenic symptoms."

The first impression gained from observation of the four main groups of psycho-somatic illness, is of the superficial similarity of the personalities encountered, in spite of varied symptoms and psychopathology. For instance, in addition to the main cardiac, dyspeptic, or rheumatic symptoms of each group, they all reported a number of other symptoms common to the four groups. Table III shows the incidence of these symptoms. The four groups are compared with the group of anxiety states which showed no main somatic localization of symptoms.

TABLE III.—DISTRIBUTION OF SYMPTOMS OVER ALL GROUPS

Symptoms complained of in addition to main complaint	313 cases effort syndrome	424 cases dyspepsia	223 cases rheumatism	122 cases headache	464 cases anxiety state
	per cent.	per cent.	per cent.	per cent.	per cent.
Breathlessness	95	21	33·4	13	48
Dizziness ..	64	54	24	91	54
Sighs ..	47	36	12	10	49
Trembling ..	72·5	63	54	18	92
Flushes ..	50	22	89	32	41
Fatiguability	90	84	72	75	68
Nervousness	67	75	12	8	57
Sweating ..	75	63·5	73	14	79
Paraesthesiæ	48	11	83	50	26
Dry mouth	43	50	9	15	43
Insomnia ..	12	27	31	25	52
Annorexia ..	15	78	10	9	48

An analysis of the case-histories to determine the precipitant of the breakdown, or, where there was no obvious immediate precipitant, of the conditions under which the breakdown took place, revealed no specific incident peculiar to one group. Moreover, the variety of precipitating causes were relatively few as is shown in Table IV. Physical trauma or the conditions of action held an unimportant place compared with severe training—e.g., O.C.T.U. or Commando—or with domestic worry, occupational worry or boredom, and it was remarkable how many patients complained that army discipline was the condition they could not tolerate. Boredom, particularly, was a fertile source of neurosis, especially when combined with some real or fancied grievance, and the high proportion of cases in artillerymen seemed to be related to employment on lonely anti-aircraft or searchlight sites. In all four groups the

previous history showed that a large proportion had had symptoms before enlistment, either continuously or at some isolated stage in their life (see Table V).

TABLE IV.—PRECIPITATING CAUSE OF BREAKDOWN

	Effort Syndrome	Dyspepsia	Rheumatism	Headache
Trauma Aircraft crash, blown up, other accidents..	per cent. 0	per cent. 2	per cent. 5	per cent. 15
Whilst in action..	2	0	0	2
Training, Commando, O.C.T.U., Assault Course..	10	8	7	6
Domestic worry..	7	9	2	21
Unsuitable occupation	11	12	11	15
Discipline ..	22	21	20	13
Boredom.. ..	45	34	28	10
Grievance ..	0	14	15	5
Infection ..	3	0	12	12

TABLE V.—PREVIOUS HISTORY OF BREAKDOWN

	Effort syndrome 313 cases	Dyspepsia 424 cases	Rheumatism 323 cases	Anxiety headache 112 cases
History of previous nervous breakdown with symptoms similar to present ..	per cent. 31	per cent. 39	per cent. 45	per cent. 31
History of previous nervous breakdown with symptoms dissimilar	10	5	16	12
Prolonged history of present condition	39	45	10	32
Cases of recent onset (since enlistment) ..	20	15	29	25*

* Mostly subsequent to trauma.

Tables IV and V, therefore, show that these soldiers developed nervous symptoms under the influence of one of the precipitants listed, but they had also reacted in a similar manner before service though they had continued in spite of them in the conditions of civilian life.

The "trigger" conditions of infection, or emotional or physical strain, which precipitate the neurosis appear to be scattered fairly equally throughout the four groups of psycho-somatic illness, but they do not account for the nature of the symptoms, which seems to depend upon other factors. These seem to be multiple; and they combine to produce an individual who will react in a certain way to a condition of stress, no matter what that condition may be. They may be physical or psychological, and are included in the following list:—

Physical

1. Heredity.
2. Constitution.
3. Previous Disease.
4. Physique-Personality.
5. Habitual Function, e.g. Habitual respiratory types of Golla and Antonvitch.
6. Autonomic Balance.
7. Endocrine Balance.

Psychological

1. Early Association.
2. Suggestion.
3. Symbolism.
4. Organ Inferiority.

These are only a few of the factors which determine a neurosis and they are those which seem to direct the location of the symptoms of a neurosis with somatic manifestations. There are many others which also influence emotional development during growth and so help to determine whether a person will become neurotic. Those which determine when he will break down are mainly environmental.

It is not possible in a short paper of this kind to discuss each factor in detail and to illustrate from this series. I propose, therefore, to discuss only some of them and to leave the remainder, to be dealt with more fully in a later publication.

Somatic Factors

1. *Heredity.*—The high incidence of cardiac neurosis in families of patients suffering from cardiac neurosis is well recognized (Wood). This, however, applies to other neuroses as well. The point is that not only is a family history of neurosis common in neurotics, but that, once neurosis becomes established in a family, succeeding generations tend, if they suffer from neurosis at all, to suffer from a similar one (see Table VI).

TABLE VI.—FAMILY HISTORY OF NEUROSIS

	Effort Syndrome	Dyspepsia	Rheumatism		Headache
			Probably organic	Probably functional	
Family history of similar neurosis ..	per cent. 52	per cent. 41	per cent. 5	per cent. 17	per cent. 43
Family history of nerves — location not necessarily the same	15	12	15	—	38

2. *Constitutional.*—All patients are placed in a physical training group on arrival in hospital, and 75 per cent. of patients do physical training during the whole of their stay. They are divided into four

classes of graded severity and a note has been kept of the performance of these 1,072 psychosomatic cases. The result shows that 71 per cent. start in the light grades and never achieve any increase in their grade. To compare the classes at work is most instructive. The two strenuous classes are full of energetic, vigorous men, who work and play with a will and join in all recreational games; the light classes are sluggish, lackadaisical, and uninterested.

Some of the acute and recent cases of anxiety recover their natural physical energy as their mental condition improves, but generally the anergia of the light classes is not due to lack of training or of exercise which will gradually be overcome, for, as stated above, the majority do not improve. Nor is it related to the medical category, for 69 per cent. of these men were in Army Category A1 on physical grounds. The physical training instructors complain that "there's not a bit of good in any of them"—meaning physical strength, co-ordination, agility; yet testing has shown that these patients as a whole are of considerably higher intelligence than a cross-section of the rest of the Army. Their disability in this direction consists of a fundamental timidity or apprehensiveness.

An inquiry into the previous histories of the entire series showed that 25 per cent. had never indulged in sports or vigorous exercise all their lives, and that a further 30 per cent., though they played games whilst at school, had lost interest or given them up in late adolescence or early in adult life. This constitutional incapacity, therefore, is not necessarily an incapacity for effort, because many of them had indulged in sport as youngsters and the condition was not confined to the effort syndrome cases. Wood (1941), investigating a series of 200 cases of effort syndrome, concluded that

"in childhood these patients are timid and delicate; they cling too long to their mother's skirts. They evade as much as possible, with the help of friendly coughs and colds; kindly doctors and soft mothers are at hand to protect them. . . . But they may not develop effort intolerance until they are ten or eleven years old, or not until much later. The case histories suggest that parental influence causes timidity and character inferiority, but not effort intolerance."

This is the impression gained from the series under review here; and a study of their case-histories as taken at the original examination confirms the fact that a very large majority of them have been timid evaders at heart for the greater part of their lives, certainly since adult age.

3. *Incidence of Previous Disease or Trauma.*—The incidence of antecedent disease as a predisposing factor in illnesses in which emotional factors play a large part has been stressed previously (1938), particularly so in asthma, for in a series of 150 cases reported elsewhere, 25 per cent. showed a history of antecedent pulmonary disease. In other words, antecedent disease leaves its mark both upon the organ it attacks and upon the patient's mind. Asthma, however, is a rare disease in this hospital and is not included in the present series.

It is interesting that trauma which long antedates the appearance of symptoms and which has often been fogotten in the interval seems to play the same part in some cases as disease does in others—for instance, the rheumatism and headache cases. The incidence of previous trauma as a factor in rheumatism and backache has been stressed previously. In the present series remote trauma was very common, particularly in the cases of backache and headache It is noticeable that the trauma was commonly in the same position as the subsequent neurotic symptom. The series is controlled against a group of 100 cases of hernia. In the controls the traumatic factor was non-existent.

TABLE VII.—INCIDENCE OF REMOTE TRAUMA

Rheumatism 223 cases				Headache 112 cases	Hernia controls 100 cases
Backache 75 cases	Generalized rheumatism 82 cases	Limbs 54 cases	Neck 12 cases		
22 (21 per cent.)	6 (7 per cent.)	8 (15 per cent.)	— — —	32 (29 per cent.)	1 (1 per cent.)

A typical history may be quoted:—

Bdr. H., aged 28. He was swept off a lorry by bough of tree in 1940—injuring his back. He was in hospital with bruises in lumbar region for ten days. There was no fracture.

He returned to duty and remained well until 1942 when he began reporting sick with backache. He was referred to the orthopædic specialist by his M.O. with a diagnosis of lumbago. The Orthopædic Specialist could find no signs of organic disease and referred him to a psychiatrist. The patient was eventually admitted to hospital.

On examination he appeared a somewhat dull and heavy looking man complaining of pain on bending or when marching. His spine was supple and no localized tenderness or fibrositic nodules were detected. No evidence of focal infection was found. X-ray of spine was normal.

For the previous 18 months the patient had been an A.A. gunner, to which arm he had been transferred from the infantry with the whole of his regiment. He disliked the work, had been moved from one part of the country to another, had stood what little action he had seen fairly well, but had been bored by the work for which he felt he was not suited. He did not get on well with the other N.C.Os. and prior to his breakdown had had his stripes taken away for insolence to a Warrant Officer. The report from his C.O. stated him to have good qualities when he liked to use them.

His work record previous to joining the Army was not a particularly good one. There had been many changes of occupation and two periods of unemployment. He had no fixed trade and had been employed mostly as a builder's labourer. At school he had been slightly below the standard for his age.

Comment.—In this case it is noticeable how the prolonged period of dissatisfaction with the patient's army occupation and the difficulties with his superiors culminated in the appearance of neurotic symptoms. Having regard to his earlier civilian history this was perhaps to be expected. Faced

with a similar situation in civilian life he would in all probability have undergone another change in occupation or another workless period. In the Army that solution was not possible, so he solved the difficulty by the production of symptoms in a part of the body which earlier experience of injury had impressed upon his mind as already damaged.

The production of symptoms by remote trauma is not exactly the same thing as the traumatic incidents immediately preceding the onset of symptoms. Trauma may act both as a predisposing factor and as a precipitating stimulus to the neurosis. This is especially so in the case of severe traumatic experiences such as bomb or shell explosions. Many soldiers who went through severe shell fire in 1940 did not develop a neurosis until two years later. The precipitating cause in these cases was sometimes another traumatic incident, but was often some completely different kind of stimulus.

4. *Physique-Personality.*—No systematic study of physique-personality has been made in the present series of cases, but it is included in the discussion for the purpose of delineating more fully the picture of psycho-somatic ætiology. The operation of this joint factor is best illustrated by the dyspeptic group. The theory has been gaining ground that peptic ulcer is simply the later stage of an emotionally or physically conditioned central process—a process which may give rise to disturbances of gastric secretion and motility. Alkan (1930), for instance, in discussing the pathogenesis of peptic ulcer, distinguishes an an-ulcerous and an ulcerous stage, and some observations by Wittkower (1931) tend to confirm this view. If this is so, then those factors which predispose to the occurrence of ulcer might be expected to be operative in an-ulcerous dyspepsia. In this connection it would seem that studies on constitution by Ruhmann (1926); Draper (1930); Draper and Touraine (1932); Cushing (1932); Einhorn (1930); Hurst and Stewart (1929); and Davies and Wilson (1937) relating to the common occurrence of gastric ulcer in the asthenic-obsessional are of great moment.

It will be interesting to see whether further studies will show that peptic ulcer is in fact a mere incident in an underlying neurotic dyspepsia. In a large number of cases in the present series it was almost impossible to diagnose clinically the presence or absence of ulcer in a dyspeptic, and the symptomatology does not seem to alter greatly with the appearance of an ulcer, at any rate in its early stages. Both of the patients in whom an ulcer was found to be present were regarded, on clinical grounds, as being free from organic lesion. Of the remaining 424 cases, 21 were thought to have gastric or duodenal ulcers and were subsequently shown to have a normal gastric mucosa. Further evidence is required both upon the proportion of functional dyspeptics who develop an ulcer later and upon patients with a confirmed ulcer which was preceded by neurotic manifestations.

This paper may be concluded by repeating that only a few of the physical aspects of psycho-somatic ætiology have been discussed and none of the psychological ones. I have stated or implied that these factors do nothing but direct the location of the symptom once the ultimate causes of neurosis have produced a favourable psychological status. The causal factors in neurosis, however, cannot be separated into isolated groups as easily as that, for the individual factors are interdependent, but such a scheme may help in the understanding of these disorders, though it may be discarded as knowledge increases.

Summary

1. 2,288 consecutive admissions to a Military Hospital for neurosis have been considered.

2. 3·4 per cent. of the cases had an organic disease. These have been briefly described.

3. The mean blood pressure of the remainder was found to be higher than the accepted normal.

4. Anomalous results of exercise tolerance test which were found are probably due to nervous factors.

5. A list of the factors which may lead to the location of psycho-somatic symptoms is given, and some of these factors, illustrated from the present series, are discussed.

My thanks are due to the Commanding Officer and staff of the hospital for their co-operation in the examination of patients.

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CAUSATION OF MONGOLISM

BY

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EVER since Dr. Langdon Down in 1866 introduced the term " Mongolism," this group of aments has been the subject of numerous investigations. But so far the cause of Mongolism remains obscure and, in spite of a growing amount of literature, it is impossible to say whether there is a single cause for all cases of Mongolism or whether various etiological factors are to be held responsible.

Careful investigation of one-hundred and thirteen Mongols—seventy-five males and thirty-eight females—admitted to this Hospital during the last twenty years has enabled me to question the validity of the causes put forward by other observers and to form my own opinion as to the probable cause.

Very valuable contributions have dealt with the influence upon Mongolism of heredity—Brushfield, Fantham, Orel; of alcoholism and syphilis—Lind, Riddel, and Stewart; lack of vitamins and hormones—Tredgold; fœtal hyperthyroidism—Clark; diminished potency of the secretion of the corpus luteum—Penrose; and infusion of racial Mongolian blood into the family—Crookshank. Shortage of space compels me just to refer to these writers and their theories and ideas.

I shall now discuss exogenous factors having direct influence upon the pregnant uterus and would subdivide them into:—

A. *Ill-health of the Mother.*
B. *The Theory of Exhaustion* (*Shuttleworth*).
C. *The Theory of Increased Amniotic Pressure.*
D. *The Theory of Nidation.*

A. *Ill-health of the Mother.*—Tredgold reported that in a large proportion of his cases there was a history of ill-health, privation or anxiety of the mother during gestation. Brushfield goes so far as to say that among his one hundred and seventy-nine cases ill-health, privation or overwork of the mother was found in 34 per cent. of the cases. This is a very high figure indeed.

Among my own ninety-eight cases in seven or 6·8 per cent. there was considerable degree of ill-health, nervousness, worry or strain during gestation and I share the opinion of former writers that, though ill-health of the mother cannot be regarded as the sole causative agent, it certainly has some influence upon the development of the Mongol.

B. *The Theory of Exhaustion.*—Shuttleworth was the first to point out that the Mongol is the product of uterine exhaustion. He was able to show that the Mongol in the majority of cases is the last born of a large family, the mother's age being rather advanced at that time. Many other observers confirmed this view.

Among ninety-seven Mongols under my observation:—

3 were only children.
18 belonged to small families of only two children.
24 to families of three or four children.
16 to families of five or six children.
36 to families of seven or over seven children.

The position of the child among the other children was:—

7 were first born.
66 last born.
15 last but one.
8 were born in between the other children.

The ages of the mothers—seventy-nine were investigated—were:—

below 20	1
between 20 and 30	14
between 31 and 35	9
between 36 and 40	32
between 41 and 50	21
between 51 and 60	2

The total over 35 being fifty-five, i.e. 70 per cent.

These data show that the majority of Mongols are the last born of rather large families, and that the age of the mother is rather advanced. I found the age thirty-eight remarkably often. On the other hand there are many young mothers among them. Some of the Mongols are first born and some belong to small families. Though the age of the mother and uterine exhaustion should not be neglected, they cannot be considered as the primary cause unless uterine exhaustion has a certain amount of influence upon the condition of the mucous membrane of the uterus with regard to the implantation of the impregnated ovum

C. *The Theory of Increased Amniotic Pressure.*—Van der Scheer thought that as a consequence of certain abnormalities of the mucous membrane of the uterus the impregnated ovum is embedded under

unhealthy conditions. This causes the formation of too narrow an amniotic sac and too high a pressure inside this sac so that even in the sixth or seventh week of embryonic life the development of the fœtus is seriously impeded. He speaks of direct and indirect amniotic pressure and of poor blood supply to important parts of the fœtus. Van der Scheer's view is actually a basis for the next theory.

D. The Theory of Nidation.—Nidation is the implantation of the impregnated normal ovum into the mucous membrane of the uterus. It is well known that during the first few weeks after impregnation, the ovum does not get its nourishment through blood vessels, but is supplied solely by the surrounding tissues through osmotic pressure or osmotic activity.

In order to guarantee an adequate supply of nourishment and through it a normal development of the fœtus, the mucous membrane at this early stage must be healthy. Any harm done to the mucous membrane shortly or relatively shortly before impregnation has taken place, be it by a toxin or by mechanical intervention, will cause an interruption of this normal vital supply to the ovum, and in certain cases may lead to a pathological development of the fœtus, in some of them to Mongolism.

Professor E. Mayerhofer from the Königliche Universitäts klinik in Zagreb has published a very interesting article in the *Annales Pediatricæ* 1939 about the causation of Mongolism. He observed among his young and well-to-do married patients that the number of first born Mongoloid children is on the increase. According to his views, these young people have no desire to have children. They, therefore, use abortifacients or the curette. When pregnancy occurs later, the first child often is a Mongol. As far as I am aware, he is the first to introduce a new term in the history of Mongolism, that of the so-called " Curettage Mongol."

Among ninety-eight Mongols I found twelve definite cases where miscarriage in the mother due to the use of abortifacients, or curettage, or miscarriage of unknown origin immediately preceded the birth of the Mongol. It should be remembered that I was dealing with people who, to some extent, are not interested in their children and were very reluctant to give any kind of information. In some cases I had the definite feeling that the mothers gave me deliberately false information. I am sure I am not wrong in assuming that the number 12 or 12·7 per cent. is a too low one and that it would have been far higher if my informants had been unbiassed. Also it should be realized that my informants belong to a class of people on whom curettage is not often performed, for they generally use abortifacients. Investigations among well to do people would probably lead to far higher figures than those mentioned in this paper. Here are some short references of my cases:—

Case 1.—A. T. W., male, aged twenty-nine. His father and mother are alive and healthy. The age of the mother at the birth of the defective was thirty-eight years.

Brothers and sisters:
1. and 2. Twins, both male, normal, now 39.
3. and 4. Twins, male and female, normal, 37.
5. Male, normal, now 36.
6. Male, normal, now 34.
7. MISCARRIAGE, through curettage.
8. *The defective.*
9. and 10. Twins, male normal, now 25.

Case 2.—A. D. M., male, aged twenty-three. The mother was forty-one at the defective's birth. A first cousin on the father's side has a boy of five who is a Mongol.

Brothers and sisters:
1. Male, now 35, normal.
2. Female, now 33, normal
3. Female, now 26, normal.
4. MISCARRIAGE, through curettage.
5. *The defective.*

Case 3.—S. G. St., male, aged twenty-four. The father and mother are both alive and healthy. An aunt of the patient is a defective. The mother was thirty-eight years old at the defective's birth.

Brothers and sisters:
1. Female, died at the age of 3 days of Peritonitis.
2. Male, now 32, normal.
3. MISCARRIAGE, caused by shock during last war.
4. *The defective.*

Case 4.—M. K., male, aged twenty. The father was thirty-nine, the mother forty-one at his birth.

Brothers and sisters:
1. Female, now 43, normal.
2. Female, now 41, normal.
3. Female, now 39, normal.
4. Female, now 37, normal.
5. Female, now 35, normal.
6. Male, now 33, normal.
7. MISCARRIAGE.
8. Female, now 31, normal.
9. Male, now 29, normal.
10. Male, died at 13 years with rheumatic fever.
11. Male, now 24, normal.
12. Male, now 21, normal.
13. MISCARRIAGE, caused by abortifacient.
14. *The defective.*

Case 5.—B. M. H., female, aged thirty-two. The mother was thirty-eight years old at her birth.

Brothers and sisters:
1. Female, now 45, normal.
2. Female, now 42, normal.
3. Male, now 39, normal.
4. Male, now 37, normal.
5. Male, now 35, normal.
6. Male, now 33, normal.
7. MISCARRIAGE.
8. MISCARRIAGE, both caused by abortifacients.
9. *The defective.*

Case 6.—G. W. B., male, aged seventeen. The mother was forty-seven at the defective's birth.

Brothers and sisters:
1. Male, now 42, normal.
2. Female, now 41, normal.
3. Male, now 35, normal.
4. Male, now 30, normal.
5. Male, died at the age of five months.
6. MISCARRIAGE, due to shock.
7. *The defective.*

Case 7.—S. N., female, aged eighteen. The father was thirty-five, the mother thirty-four at her birth.

Brothers and sisters:
1. Female, now 28, normal.
2. Female, now 25, normal.
3. MISCARRIAGE, after five months, due to shock.
4. *The defective.*

Case 8.—C. S. G., female, aged twenty-seven. The mother was forty-eight years old at her birth.

Brothers and sisters:

1. Male, normal.
2. Female, died of Tuberculosis after whooping cough.
3. Male, normal.
4. Male, normal.
5. Male, normal.
6. Male, normal.
7. Male, died of Meningitis after whooping cough.
8. Male, normal.
9. MISCARRIAGE, reason unknown.
10. *The defective.*

Case 9.—R. J. B., male, aged twenty-three. The father was thirty-six, the mother thirty-nine at his birth.

Brothers and sisters:

1. Male, normal.
2. Female, normal.
3. Male, normal.
4. Female, normal.
5. Female, normal.
6. MISCARRIAGE, caused by curettage.
7. *The defective.*

Case 10.—A. J. B., male, aged thirty. The father was forty two, the mother forty at the defective's birth.

1. MISCARRIAGE.
2. Stillbirth.
3. Died at two weeks of " uræmic convulsions."
4. *The defective.*

I presume though I could not prove it that parental syphilis was in this last instance the cause of the miscarriage and the stillbirth.

Besides the twelve cases where miscarriage immediately preceded the birth of the defective which could be established beyond doubt, I would like to cite another case.

Case 11.—W. B. Th., male, aged sixteen.

Brothers and sisters:

1. Female, now 29, normal.
2. Male, now 28, normal.
3. *The defective.*

The mother who was thirty-six at the defective's birth, had a prolapse of the uterus previous to the birth of the defective.

In all these cases we see normal births and normal children until a miscarriage has taken place, and the birth of a Mongol after a miscarriage. It is irrelevant whether the miscarriage was caused by mechanical intervention—curettage, by intake of irritants—abortifacients, or was caused by shock or by syphilis. In all these cases I could ascertain that the birth of the Mongol following such a miscarriage took place approximately one year later which would mean that the implantation of the new ovum took place only a few months after the miscarriage.

As has already been pointed out, miscarriage causes a serious alteration of the mucous membrane of the uterus, especially in persons with a morbid heredity. Here the implanted ovum will find pathological conditions, its nourishment will be seriously hampered, and within the first few weeks of fœtal life the foundation for a Mongolian child will be laid. Apart from morbid heredity, ill-health of the mother, strain, overwork or any other cause which would interfere with the health and thus lower the normal resistance of the tissues, will contribute towards this condition.

It is, of course, difficult to assess what time is needed to restore normal conditions in a tissue which has suffered through toxins or mechanical intervention. In some persons, especially in healthy and fairly young ones, healing may be rapid and the implantation of the new ovum will take place under conditions favourable to its nutrition. If, on the other hand, many births have preceded the miscarriage, or the healing tendency of the tissues is slowed down by toxins, syphilis or anything else, a long time may elapse before normal conditions are restored.

How far, and whether at all, the prolapse in my last case influenced the birth of the Mongolian child, I am unable to say. I mentioned this case in connection with my other cases as a matter of interest.

Summary

In a review of over one hundred cases of Mongolism I have tried to form an opinion as to the cause of this amentia. Based on morbid heredity, the unhealthy condition of the mucous membrane of the uterus at the time of the implantation of the impregnated ovum seems to me to be the chief cause of Mongolism. One of the main factors contributing to this unhealthy condition is miscarriage, irrelevant whether brought about by curettage or by the use of abortifacients.

I wish to thank Dr. Edmund Nobel who has inspired me to investigate Mongolism and has given me valuable advice. I am also indebted to the Med. Superintendent Dr. T. Lindsay, the Deputy Med. Superintendent Dr. D. P. Firmin, and to Dr. D. Bryan of the above Hospital for giving me their help and advice.

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A CASE OF PARTIAL CONGENITAL HEMI-HYPERTROPHY

BY

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HEMI-HYPERTROPHY, or abnormal enlargement of one side of the body, is of interest because of its varied forms and its frequent association with other congenital abnormalities, including mental deficiency. Wagner reported a case in 1839, and in the ensuing century about a hundred cases of partial or complete hemi-hypertrophy have been recorded.

A brief description of the following case of hemi-hypertrophy, associated with Von Recklinghausen's disease, will serve as a basis for discussion.

Case report.—A male, L. G., aged 39 years, was admitted as a feebleminded patient to Leavesden Hospital in 1931. He was the second of three children of whom the others died of tuberculosis in their first year. As a child he had measles and whooping cough. He began to talk and walk at 2½ years. At 8 years he fractured his right clavicle and he says that it was after this that the difference in size of his two arms became noticeable. He attended a primary school for four years, became tuberculous and was admitted to a special school for mental defectives in 1903.

Both parents are dead and no history of the family is available.

The patient is a feeble-minded adult, with a mental age of 6 5/12 years by Burt's revision of the Binet-Simon scale. With performance tests (Drever and Collins) he has a mental age of 8 years. He is well behaved, and a good ward worker, and makes woollen rugs in his spare time.

Physical examination.—Height 4 ft. 9 in. Weight 7 st. 9 lb. Although short in stature, he is disproportionately broad, with a " Punchinello " type of thorax. There is marked difference in the length and girth of the arms, and, in a lesser degree, of the legs. The disproportion is indicated in the following table:—

	RIGHT	LEFT
Arm, length	66·5 cm.	70·5 cm.
Upper arm, girth	23 ,,	25 ,,
Forearm, length	40 ,,	42·5 ,,
Forearm, girth	23 ,,	25 ,,
Middle finger, length ..	10 ,,	10·7 ,,
Hand, girth	19·5 ,,	21 ,,
Leg, length	77·5 ,,	78·5 ,,
Thigh, girth	42 ,,	43 ,,
Foot, length	21·5 ,,	22 ,,
Dynamometer, hand ..	100	80

The difference between the upper arms is very noticeable (Fig. 1). The left shoulder and scapular region are larger in all dimensions than the right, and this difference is seen in both osseous and muscular tissues. The deltoid, trapezius and pectoralis major muscles stand out, and the enlarged muscles are firm to the touch, but, in spite of their appearances, when tested with the dynamometer and by movements against resistance, it can readily be demonstrated that they are actually weaker than those on the normal right side.

When the patient stands erect, the left shoulder is on a higher plane than the right. There is no limitation of movement in the joints of the four limbs. There is, however, considerable limitation of movement in the cervical spine in all directions; lateral movement is slight and extension of the neck is so limited that in the supine position the occiput remains at a height of several inches from the floor. When the patient is asked to direct his gaze to the ceiling, upward movement of the eyes is not accompanied by any extension of the head (see Fig. 1).

There is marked mid-dorsal kyphosis. The thorax shows a depression below the manubrium sterni, and respiratory movements of the chest wall are small.

Chest examination shows the following abnormal findings: poor movement, dullness to percussion at both apices, and poor air entry throughout. X-ray shows fibro-caseous tuberculosis at both apices. Temperature and pulse are normal, his weight is steady and he has no cough or sputum. The heart and abdomen reveal no abnormal findings. Blood-pressure is 105/65. The cranial nerves are normal, except that both pupils are small and eccentric, and react sluggishly to light and on accommodation, and that the cornea of the right eye shows an old traumatic central opacity.

The left arm, though larger, is weaker than the right; no difference in motor power can be detected in the legs. Sensation is normal throughout. The tendon jerks are all brisk and equal, the abdominal reflexes absent, the plantars flexor. Sexual development is less than normal, but the testes are of equal size. On the trunk there are two large and several small *cafe-au-lait* areas of pigmentation. On the left forearm there was one subcutaneous nodule, which was removed for microscopic examination. This proved to have the relatively cellular structure of a soft fibroma.

Biochemical investigation

Blood Wassermann, Negative.
Serum calcium =8·4 mgm. per cent.
Serum inorganic phosphorus =1·9 mgm. per cent.
Serum phosphatase =4·5 units.

Radiological examination

1. The skull is symmetrical in its two halves and the bones of the vault are of equal density and thickness on the two sides. There is no indication of acoustic or other neurofibromatous tumours.

2. The vertebral column shows marked kyphosis and osteoporosis, and the intervertebral disc spaces are diminished. There is calcification of the anterior vertebral and interspinous ligaments.

3. The humerus and hand. The left humerus, the radius and ulna, and the bones of the left hand are shown to be definitely larger than the right (Fig. 2).

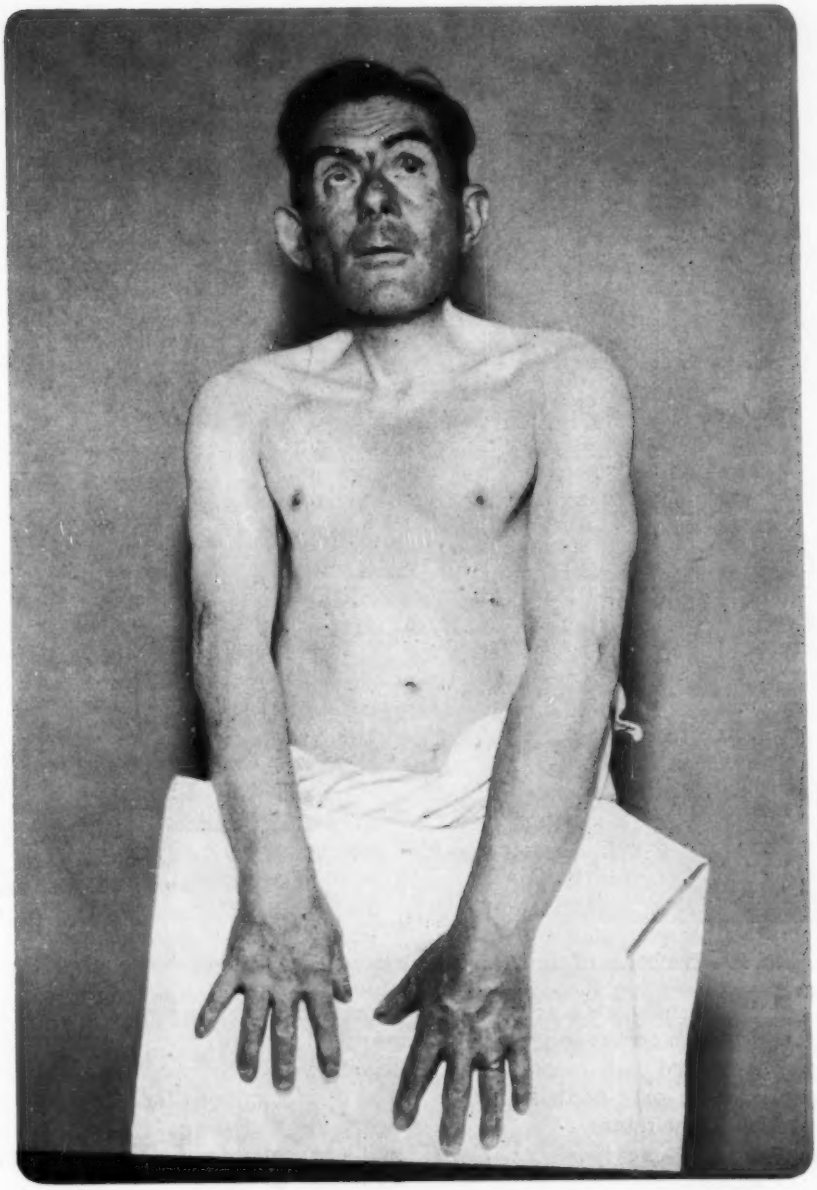

FIG. 1.—Note enlargement of left upper limb, limb girdle. There is marked prominence of the left pectoral and deltoid muscels. Patient is endeavouring to look upwards.

Discussion

The asymmetry in this patient cannot be due to muscular atrophy of the limbs of the right side of the body such as that found in mild forms of infantile cerebral hemiplegia, for in this case the muscles show no evidence of wasting and although smaller than those of the left side are definitely more powerful. Furthermore, there is entire absence of signs of neurological involvement of the cortico-spinal motor path. Likewise the preservation of normal cutaneous and deep sensibility excludes the possibility that the case has a syringomyelic origin similar to that reported by Guillain *et al.* (1925). Again, in pseudohypertrophic muscular dystrophy, the hypertrophy is bilateral, hypertrophy is most evident in the legs and the affected limbs do not show enlargement of the bones. In the very rare disease dystrophia musculorum hyperplastica, there may be rarefaction of bone, but never enlargement.

In the case now reported, the enlargement on the affected side involves both osseous and muscular tissues, and has points of resemblance with cases reported to be congenital in origin. In those which have come to autopsy (Gesell, 1921), it has been found that the increase in muscle bulk is due to an overgrowth of connective tissue.

The presence on the patient of several *cafe-au-lait* patches, a single subcutaneous fibroma, and the associated kyphoscoliosis with calcification of the anterior vertebral ligament and interspinous ligaments are consistent with the view that this is a case of von Recklinghausen's neurofibromatosis, a disease in which disturbances of growth are known to occur. Whether the associated mental defect is

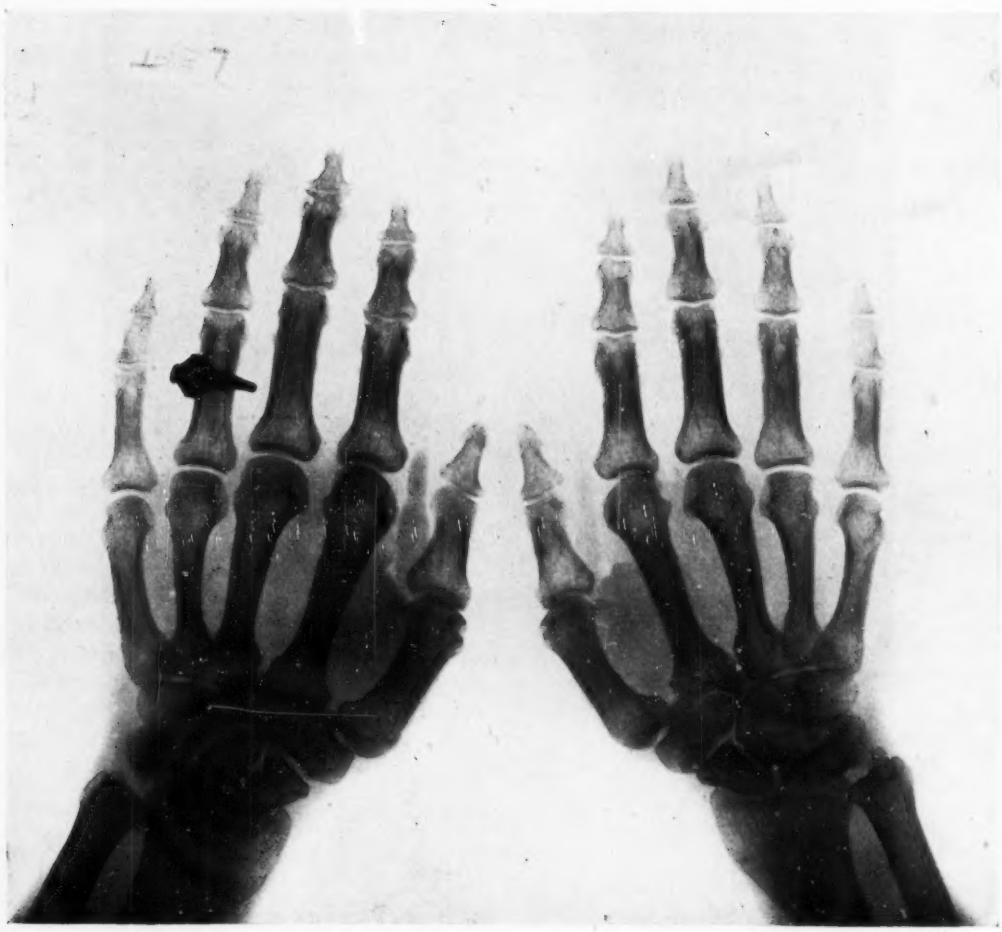

FIG. 2.—The bones of the left hand are larger than those of the right hand.

merely fortuitous, or is a consequence either of a diffuse cerebral sclerosis which occurs in some cases of hemi-hypertrophy associated with mental defect, or of a cerebral gliosis which may occur in neurofibromatosis, must be left to the future.

Summary

The case here reported presents two congenital anomalies—congenital hypertrophy, and von Recklinghausen's disease. The left shoulder, left arm and hand, left leg and foot, are all larger than the right, but they are also definitely weaker. There is no evidence of syringomyelia, congenital hemiplegia, or pseudohypertrophy. Evidences of von Recklinghausen's disease are dorsal kyphoscoliosis, calcification of interspinous and anteri or common vertebral ligaments, *cafe-au-lait* pigmentation on the body, and a neurofibroma. The mental deficiency may be idiopathic or may be accentuated by, or due to, one or both of the congenital anomalies present.

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POST-TRAUMATIC PAIN AND THE CAUSALGIC SYNDROME

BY

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IT is not uncommon, especially in wartime, to be faced by patients complaining of persistant severe pain in the hand or foot following an injury to a limb, despite the absence of apparent cause. It is with such cases that the present paper is concerned. Excluded from consideration are cases in which post-traumatic pain arises from tender neuromata or obvious vascular abnormalities.

Weir Mitchell (1872) dealing particularly with injuries involving nerves used the term causalgia for this condition, and though describing many examples that have become classical he did not rigidly define the term. Indeed Homans (1939) suggests that a considerable number of states have been at one time or another included under this term and such a view is supported by ideas developed elsewhere (Doupe and Cullen 1943). On the other hand, it would seem that cases of causalgia have been described under a variety of other names. This tendency to dispersion in the literature has been noted, both by Homans (1939) and de Takats (1943), and they have been tempted to counteract it by grouping many of these conditions together. In Table I it will be seen that there is a disparity in the conditions so grouped by these two authors and that the cause of this disparity appears to lie not only in the redundant terminology but in different conceptions of the genesis of the condition: Homans stressing the part played by reflex arterial spasm while de Takats is impressed by the element of vasodilatation.

TABLE I

HOMANS, 1939	DE TAKATS, 1943
Reflex Arterial Spasm.	État Physiopathique of Vulpian.
Chronic Segmental Arterial Spasm.	Causalgia.
Causalgia.	Sudeck's Atrophy.
Reflex Dystrophy of the Extremities.	Post - Traumatic Painful Osteoporosis.
Trophic Œdema.	Peripheral Acute Trophoneurosis.
Traumatic Osteoporosis.	Chronic Traumatic Œdema.

Grouping of Terms applied to Post-Traumatic States.

The confusion caused by using the term causalgia for different conditions and by describing cases of causalgia under different names indicates the need for the classification and segregation of different post-traumatic painful states. However, a classification, no matter how sorely needed, cannot be satisfactory so long as it is based on symptoms. As it would be over ambitious to attempt to define the post-traumatic states themselves it is the intention here merely to distinguish the different varieties of pain and to speculate as to their cause. In this way the value and the limitation of the symptom of pain in differentiating the various post-traumatic states will become evident.

In this paper a group of patients with a variety of post-traumatic pains will be presented and a special attempt will be made to define one particular type. This for valid historical reasons will be called the causalgic syndrome and despite the rules against tautology, the cases will be said to suffer from causalgic pain. Personal considerations suggest that this usage is free from the dangers of spurious finality which are inherent in a diagnosis of " causalgia." Cases of other than the causalgic syndrome have been included as a means of contrast and to illustrate the three most common types of post-traumatic pain. As the group of cases has been selected for this purpose it does not show the relative incidence of the particular syndrome. The description of causalgic pain may best be accomplished by presenting a theory of the mechanism by which it is produced. In developing the theory one of several manifestations could be used as a starting-point and it might seem that the objective findings would prove the most satisfactory. The objective findings consist of changes in vascularity and nutrition and it will be well to consider how far a study of them can aid in the present endeavour.

The vascular changes have been studied most recently and most thoroughly by Miller and de Takats (1942), who find, in agreement with others (Leriche and Fontaine, 1929; Lewis, 1942), that the blood-flow is greater in the painful than in the normal contralateral extremity. The importance of such observations naturally depend on the ability to interpret them. The blood-flow to normal digits may change a hundred-fold or more (Wilkins *et al.*, 1938), while the factors affecting the flow are too numerous to detail. Lewis and Pickering (1931–33)

* Working on behalf of the Medical Research Council.

have studied some of these and find that differences in use, posture, and temperature can cause unequal flows in normal limbs. Therefore, it may be thought that numerous interpretations could be placed on the finding of an increased flow in an injured extremity which, because of œdema, lack of use and general disturbance of function, is hardly comparable to the normal. The number of possible interpretations is also increased if there is a co-existing nerve injury. This difficulty of interpretation is demonstrated by the charts of skin temperatures in Figs. 2, 4, 6, and 8, which confirm the findings of an increased blood-flow in the affected extremities, but seem rather to ask for an explanation than to suggest one. Thus it is concluded that the finding of an increased blood-flow or an increased oscillometric index does not contribute to the understanding of the primary mechanism of the causalgic syndrome. This conforms with the opinion of White and Smithwick (1943), who state: "All that emerges from these theories as reasonably certain is that abnormal vasomotor activity usually accompanies pain."

The nutritional state of the extremity has caused comment since the first description of glossy fingers by Paget (1864). Mitchell *et al.* (1864*a*) were particularly impressed by these changes, but note that pain may be present without the cutaneous disorder. Lewis (1942) remarks that some of the changes may be due to disuse while reference to Hurst's (1940) description of the results of hysterical palsies suggests that many of the features may be so explained. It is to be noted that case D. P. was a well-marked example of glossy skin and curved nails, yet he was free from pain. Pollock and Davis (1933) report similar experiences. Thus the exact significance of the skin-changes is debatable.

Besides changes in the skin, changes have been described in the bones and these are so striking that they have achieved pride of place in some terminologies, viz., the post-traumatic painful osteoporosis of Leriche and Fontaine (1930), Fontaine and Herrmann (1933), and Herrmann *et al.* (1942). It would appear that these authors regard the bone-changes as being diagnostic of this condition, but the view is gaining ground that the spotty atrophy is a non-specific reaction of bones and de Takats (1943) emphasizes that the diagnosis cannot be made by X-rays alone. This point is illustrated by cases W. C., D. P., and F. B. in the present series, who showed well-marked osteoporotic changes yet had slight or no pain. Delorme (1917) has also presented evidence for this view. To many (Noble and Hauser, 1926; Gurd, 1934; Nonne, 1902; Sudeck, 1938; Kienbock, 1901; and Turner, 1936) the porotic picture of the bones in the acute stage has suggested that it is produced by nervous action. That such an explanation is not tenable is shown by cases R. D., W. A., and D. P., in which the course of the bone atrophy was not altered by the degeneration of the nerves. The ulnar nerve was completely divided in the first two cases, the median and radial in the last. It seems that the disturbances of bone, like those of the skin, may be present with or without pain, with or without a nerve supply. Therefore, they fail to give a clue to the primary disturbance in the causalgic state.

At first sight it might appear unsatisfactory to be forced to depend upon a subjective symptom such as pain for the basis of investigation. Nevertheless, pain is the central feature of the causalgic syndrome and as such would in any event merit consideration, but so unique are its features that they command attention. These features have been exceptionally well summarized in the publication of the Medical Research Council (1920) which states: "Causalgic pain has the following characters. It is (1) spontaneous; (2) hot and burning in character, intense, diffuse, persistent, but subject to exacerbations. (3) Causalgic pain can be excited by stimulation, which does not necessarily produce a physical effect on the limb. Emotional excitement usually aggravates the pain and brings on a paroxysm. (4) It tends to lead to profound changes in the emotional state of the patient." To these may be added a fifth characterisitc, that of relief by sympathetic block. This combination would appear to permit of only one explanation and for the proper evaluation of this explanation the following statements should first be considered.

(A) In certain conditions nerve impulses can alter the excitability of adjacent fibres. This has been shown by Katz and Schmitt (1942). Moreover, Young (1944) has found evidence that the substance of neighbouring axons may sometimes fuse, at least temporarily, during regeneration, while Speidel (1935) has observed the actual occurrence of such a fusion in his frog preparations.

(B) Sympathetic fibres to the digital vessels and to the palmar and plantar sweat glands are actuated by emotional stress. Sympathetic fibres are also brought into activity by the needs of thermoregulation, vasoconstrictor fibres in case of undue heat loss, sudomotor fibres in case of undue heat gain. Pilomotor fibres are similarly actuated by a variety of stimuli, some of which include cold, emotion, micturition, defæcation, and certain forms of cutaneous stimulation.

These two statements forcibly suggest the possibility that causalgic pain is due to the activation of sensory fibres by sympathetic impulses. In support of this proposition it will be found that it furnishes an explanation for the various qualities of causalgic pain.

(1) The pain would seem to be spontaneous in that it would be in part related to the needs of thermoregulation rather than to any external or local influence. Due to alternating activities of the sudomotor and vasoconstrictor fibres pain would be present both when the subject is hot and when he is cold. It might be expected, however, that changes in intensity of the spontaneous pain would be produced by changing the need for heat conservation to that for heat dissipation. The four attempts that were made to demonstrate this resulted in the records shown in Fig. 2, Exps. 1 and 2;

Fig. 6, Exp. 1; and Fig. 8, Exp. 1. In these experiments with the exception of that reported in Fig. 6, Exp. 1, the patients reported a diminution of pain when release of vasoconstriction was occurring and before sweating was observed. These results, while suggestive, must be interpreted cautiously, not only because the amount of pain cannot be accurately assessed, but because the pain would be expected to vary with the " feeling tone " which is itself altered by changing from the cold to the hot state.

(2) The pain would be diffuse, i.e. not well localized, and if pain and temperature fibres being small were particularly sensitive to the temporal configuration of the action currents of the sympathetic fibres, the sensation would be described as hot and burning. Moreover, the sensation would be foreign to previous experience, and this would account for the great difficulty found in describing its nature (Cases F. L. and M. S.). It will be noted that in cases E. M., A. B., W. A., and W. E. it was described as a burning or searing feeling.

(3) Emotional excitement or stimulation which does not necessarily produce an effect on the limb would cause pain because of the associated discharge in sympathetic fibres. This characteristic of causalgic pain which is so unique is easily demonstrated by the simple procedure of asking the patient to take a deep breath. In cases T. P., A. B., M. S., and W. E., to whom this was done, a momentary exacerbation of the pain was experienced, and this can be related to the increased activity of vasoconstrictor fibres (Bolton *et al.*, 1936) and sudomotor fibres (Carmichael *et al.*, 1941) caused by a deep breath. It is to be noted that another type of stimulation, namely, a pin-prick, anywhere on the body has been shown to cause a similar sympathetic discharge (Stürup *et al.*, 1935), and this likewise produces the pain. In this instance the time relations are ascertainable, and it has been found (Fig. 1) that the exacerbation of pain commences 1–2 seconds after the pin-prick, i.e. coincident with the discharge rather than with the vasoconstrictor or sudomotor activity. Such a phenomenon no doubt accounts for much of the hyperæsthesia found when the causalgic limbs are examined which contrasts with the liberty with which some patients can themselves touch the parts. In fact, in cases T. P. and E. M. the mere apprehension of being touched was associated with a notable increase in the pain. Moreover, causalgic pain differs from other pains in that it may be aggravated rather than relieved by having the attention firmly focussed elsewhere. This can be seen in cases T. P., E. M., and W. A., in whom it may be thought that the diversions of the cinema were accompanied by emotional excitement with consequent sympathetic discharge leading to an increase in pain.

(4) The tendency to profound mental changes would be the least surprising consequence of pain produced in this fashion. The patient would be caught in a cycle of peculiar viciousness, pain, and worry leading to sympathetic discharge, causing further pain and worry, a train of events which might well lead the unfortunate sufferer to seek solace by the most desperate measures. However, some of the indications of mental disturbance, such as a desire for solitude and phobias directed towards noises, etc., can be explained without hypothecating any mental derangement. Thus cases T. P., E. M., F. L., and A. B. preferred to be left alone and to lie cuddled in their beds in a quiet corner of the ward because social contacts inevitably led to pain. It is noteworthy that these reclusive traits disappeared immediately the pain had been stopped by sympathectomy. Likewise, the fear of noises which superficially would appear quite unreasonable is explained by the sympathetic discharge caused by this stimulus (Stürup *et al.*, 1935). It may also be postulated that the curious apprehension of dry contact elsewhere on the body (cases A. B. and M. S.) is connected with sympathetic discharges possibly in pilomotor fibres. Moreover, the soil is prepared for the cultivation of a variety of conditioned responses, for once a situation becomes associated for any reason in the patient's mind with an increase in the pain, recurrence of the situation will cause apprehension which in turn will induce a sympathetic discharge producing the feared pain.

(5) It is obvious that a sympathetic block would abolish causalgic pain and the efficiency of this measure is seen in all the cases of the causalgic syndrome. Three other explanations for the phenomenon may be considered. (1) Lewis (1942) has suggested that the vasodilatation so produced is the cause of the relief. This, however, is unacceptable because vasodilatation produced in other ways, i.e. reflexly, does not abolish the pain (cases T. P., E. M., A. B., and M. S.). (2) de Takats (1943) considers that it is efficacious because it causes arteriolar dilatation which is associated with a capillary constriction and thus corrects what he claims is the primary disturbance. In support of this he mentions that the pulsating pain is abolished by suprasystolic compression of the limb. Such a procedure had no effect on the pain in case A. B., and cases with pain pulsating in rhythm with the heart have not been encountered. This explanation, therefore, does not seem satisfactory for the causalgic syndrome, but there may well be other members of the group of the post-traumatic pains to which this or some related theory is applicable. (3) Middleton and Bruce (1933–34) considered that pain is relieved by sympathectomy because the afferent pain pathways are cut. Despite the lack of evidence for afferent fibres in the sympathetic nerves to the limbs this hypothesis was tested in case T. P. by a spinal anæsthetic which blocked the posterior root inflow from the feet as shown by the loss of sensation, but did not affect the sympathetic outflow as shown by the maintained low skin temperature (Fig. 2, Exp. 4). This resulted in a complete cessation of pain showing that the segmental inflow was requisite for the appreciation of causalgic pain. Therefore, in default of other explanations and because the present one seems to fit the case so aptly it is considered that sympathectomy causes relief

by blocking the efferent impulses which would otherwise stimulate the sensory nerves.

So far this line of reasoning has encountered no pitfalls, but the observation of Tinel (1918) that the pain is relieved by blocking the nerve below the lesion appears to present an impasse. In reality this discovery forms the basis on which some of the causalgic states following nerve injuries can be brought into line with those which follow injuries not primarily involving the nerves. In cases such as A. B., M. S., and W. A., where nerve block below the level of the injury relieved the pain, it must be presumed that the conjunction of the sympathetic fibres and the sensory fibres occurs in the periphery. Nor is it difficult to imagine how certain circumstances of œdema and ischæmia could impair the nutrition of the terminal nerves so that through defective insulation or actual union of the fibres cross stimulation could occur. It is a defect of the present series of cases that it contains no instance of the causalgic syndrome following injuries other than those involving nerves, though it must be admitted that a review of cases, such as that of A. B., indicates that there was little evidence of primary nerve involvement. Retrospection suggests that a nerve lesion had been presumed in order to account for the pain. In other cases of injuries to the nerves the site of the transference of the impulses lies at the place of injury, as shown by the failure to relieve the pain by nerve block below the lesion (cases T. P. and E. M.). This would appear of necessity to be the condition underlying the causalgic pains of phantom limbs (case W. E.).

It is obvious that this thesis is open to clear-cut proof or disproof by the crucial experiment of stimulating the distal end of the sympathetic nerves supplying the causalgic part. In practise the procedure is difficult, due to the complications introduced by the anæsthetic. It was attempted in two cases, and faradization of the end of the chain evoked expressions of pain which were too vaguely localized to have great importance attributed to them.

It has been pointed out above that the objective signs of the causalgic syndrome are susceptible to so many explanations that they can be made to support nearly any theory. Therefore, it is only just worth noting that they are not incompatible with the present explanation. Thus, the stimulation of the afferent fibres would cause anti-dromic vasodilatation and account for the observed increase in blood-flow. The pink shining skin might well be simply an expression of disuse plus vasodilatation.

The changes in the bones have been discussed above and are considered to be a non-specific reaction common to many different states, not all of which are painful. Another objective phenomenon sometimes encountered is hyperhydrosis. This is difficult to explain by any theory, but it is to be noted that it is not restricted to the causalgic syndrome (case D. P.). It may be that it is simply an expression of the hypersensitivity of partially denervated glands, but in any case it is not an integral part of the syndrome as it was absent in cases T. P. and E. M.

Several therapeutic procedures require mention because of their bearing on the present theory. Mumford (1938) has reported that a small amount of X-ray treatment to the hand or foot gave great relief of pain in a condition called acute osteoporosis. He suggests that the radiation may have some effect on the nerves. This therapy might therefore have been expected to benefit patients in whom a tenous junction between the sympathetic and sensory fibres was thought to be located at the periphery of the limb (cases A. B., M. A., and W. A.). In other cases (T. P. and E. M.) in which the connection was presumed to exist in the nerve trunk this treatment would be of no avail unless directed to this site. It will be seen that no benefit resulted in this series with the possible exception of case W. A. and it should be mentioned that Mumford's cases were not typical of the causalgic syndrome. This bid to obtain support for the present theory must therefore be counted a failure.

Experience of the value of periarteral sympathectomy in patients with the causalgic syndrome has been limited to case W. A. to whom no benefit accrued.

Repeated severe blistering was found by Mitchell *et al.* (1864*b*) to be beneficial in some cases, and it is not impossible that this therapy is non-specific in that it would cause a profound disturbance of the tissues leading to a disruption of any painful process that might exist. No cases have been treated by this method.

Finally, in this discussion of the mechanism of causalgic pain reference must be made to two unexplained phenomena. These are the variable time of onset of the pain and the tendency for the pain gradually to lessen. Both these must depend on the nature of the link between the sympathetic and the sensory fibres. Inasmuch as this link is a mere postulate to fit the facts, nothing in reality being known about it, there are no grounds on which to base a discussion. For the sake of clarity it should be pointed out that the long delay in onset in case W. A., is referable to the temporary abolition of conduction in the nerves.

Observations

The foregoing comments supply a key to the understanding of the cases about to be reported. In most instances the significance of the observations will be too apparent to require formal interpretation. The terminology is discussed in the following section.

The methods used to obtain the experimental observations are described in a former paper (Doupe, 1943). To obtain the X-rays a standard technique was used, and with few exceptions the normal and affected limbs were simultaneously exposed. In the reproductions the normal has been omitted in some instances to save space. X-rays were taken, when possible, at intervals of one to two months, but only the more significant are shown here. All cases have

been followed for at least four months after sympathectomy.

T. P., aged 23. *A Case of the Proximal Causalgic Syndrome.*

He was admitted 9 months after incurring a gun-shot wound of the left popliteal space at El Alamein. A suture of the left external popliteal nerve had been performed in the third month.

He complained of pain and tenderness of the left foot located chiefly in the sole at the base of the outer toes. The pain commenced 3 to 4 days after the injury and rapidly became worse so that on the fifth day it was at its height and he required morphine for 5 to 6 weeks. Thereafter it somewhat diminished and following the operation in the third month he was able to sleep. In the next few months further improvement occurred, but for the last three months the condition had been stationary. The character of the pain had not altered, the sensation being that of someone tearing the toes apart. At times there were periodic exacerbations described as burning stabs occurring every 5 to 6 seconds and lasting about 2 seconds. As to aggravating factors, he had no memory of the first few months, but stated that now the tearing pain was nearly absent when lying quietly, but that he got a spasm of pain if the bed was unexpectedly jarred or if there was a sudden noise. When asked if he went to the cinema, he replied that he didn't because if there was anything exciting like " people climbing up cliffs " the pain was made worse. The pain tended to be worse in damp weather, but was immediately relieved by putting the foot in warm water. It was also aggravated by a dependent position of the leg.

Examination showed the signs of a complete lesion of the lateral popliteal nerve. The muscles supplied by the medial popliteal nerve contracted with moderate strength. Sensation was difficult to test because he resented any disturbance of the foot. He stated that the tenderness now was not so severe as at first, but he still could not tolerate any pressure. Slight touches in the distribution of the medial popliteal nerve were felt as painful, while pin-pricks were very painful. These modes of stimulation produced aggravation of his usual type of pain, and he said that he felt the pain when he saw anyone about to touch the foot. Questioning revealed that the pain caused by a threat to touch the foot did not come on at once and estimations of the delay showed this to be in the region of 1 to 2 seconds. A pin-prick on the arm, a sudden noise, or a deep breath also caused the pain

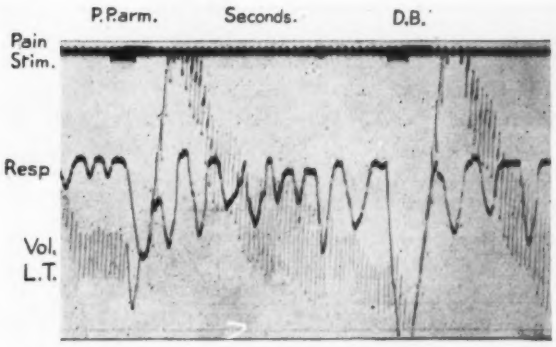

FIG. 1.—Plethysmographic record of T.P. (method of Bolton *et al.*, 1936). The upper signal activated by the patient indicates pain felt in the right foot. The lower signal indicates the stimuli, the first being several pin-pricks on the arm and the latter a deep breath. Time is in seconds. In the respiratory tracing a downstroke indicates inspiration. The volume of the left great toe is being used to show vasoconstrictor activity. An upward movement of the tracing represents a decrease in volume.

in the foot after a delay of 1 to 2 seconds (Fig. 1). He stated that he could handle the foot himself much more freely than if it were done in a similar way by another person.

The appearance of the foot was not strikingly abnormal. It tended to become œdematous if allowed to hang down for long periods, and the skin of the sole was free from callosities. The temperature of the foot (see charts in Fig. 2) tended to be slightly above those of the normal foot even after prolonged exposure. The pulse of the posterior and anterior tibial arteries of the two feet were similar to palpation. There was considerable restriction of movement at the ankle and at all the joints of the foot. X-rays of the two feet showed a well-marked decalcification of the affected foot, suggestive of the latter stages of Sudeck's atrophy (Fig. 3).

At the tenth month, i.e. 1 month after admission, the condition being unchanged, the wound was explored. The state of the lateral popliteal nerve required excision of a length of 5 cm. and re-suture was performed. The medial popliteal nerve was found to be the seat of a slight

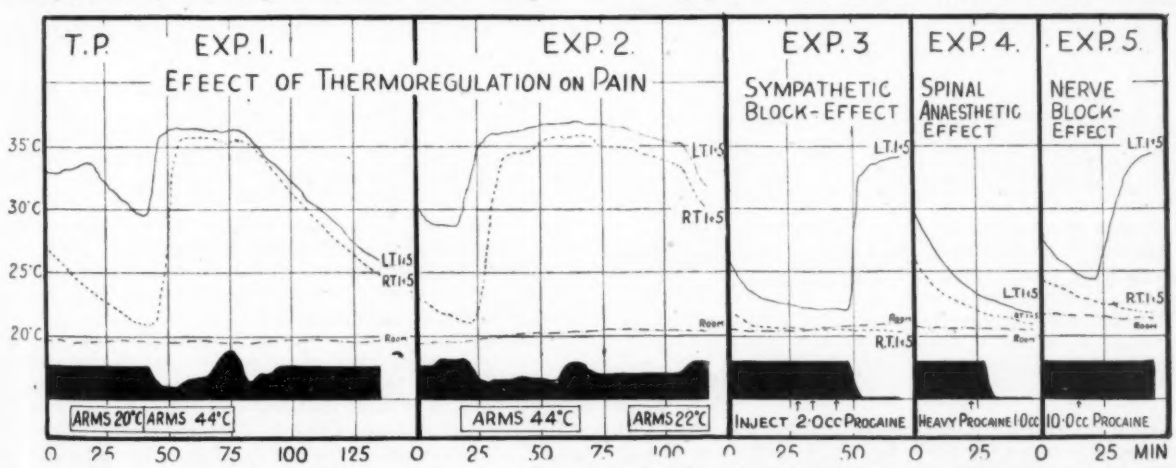

FIG. 2.—Temperature charts of subject T.P. In this and similar figures the following conventions are used. The continuous line represents the temperature of the tip of the affected digits, the broken line that of the contralateral digits and a broken line with dots that of the room. In those instances in which the affected digits behaved discordantly a dotted line is used to represent one of them. The symbols LT 1 and 5, etc., denote the left first and fifth toes, etc. Temperature readings were taken at all sites at 3-minute intervals. The filled area represents the degree of pain as assessed from the patient's statements at 5 to 10-minute intervals in relation to the pain at the beginning of the experiment. Experimental procedures are indicated on the face of the charts. Thus, in Exp. 1 the arms were put in water at 20° C. for the time indicated by the block, and were then transferred to water at 44° C. The arrows indicate the times of injections of the amounts of the anæsthetic specified.

FIG. 3.—X-ray of both feet of subject T.P. taken 12 months after injury.

fusiform thickening about 3 cm. in length, which was adherent to scar tissue and to the neuroma on the lateral popliteal nerve. Faradic stimulation of this area produced the pain in the foot. Neurolysis was performed and the nerve placed in a bed deep in the popliteal space. The pain was in no way affected by this operation, and consequently when the plasters were removed a course of X-ray therapy was given to the foot. This also had no effect and 6 weeks later the following investigations were performed:—

1. Block of the left lumbar sympathetic chain (Fig. 2, Exp. 3) relieved all pain and most of the tenderness. To rule out a psychogenic element the procedure was repeated, but the chain was not blocked, as shown by the maintenance of vasoconstriction, nor was the pain in any way affected.
2. A spinal anæsthetic blocking the segmental inflow as high as L.3 completely abolished the pain (Fig. 2, Exp. 4).
3. Block of the post-tibial nerve near the ankle had no effect on either the spontaneous pain or on that induced by loud noises, though the whole foot was anæsthetic and could be handled at liberty (Fig. 2, Exp. 5).

These observations indicated that the pain was arising at the site of the nerve lesion, was being conducted by the segmental posterior roots, and that intact sympathetic pathways were requisite for the production of pain.

On the fifteenth month after the injury a left lumbar sympathetic ganglionectomy was performed. This resulted in complete relief from pain and the hyperæsthesia of the foot was replaced by a mere alteration of sensation.

E. M., aged 36. *A Case of the Proximal Causalgic Syndrome.*

Admitted four months after a bomb splinter wound of the left axilla. The notes state that the wound was explored 14 hours later, and that the brachial artery was found to be thrombosed while the ulnar and median nerves were slightly bruised. The pulse returned at the end of 2 months, the wound was infected and healing was not complete for three months.

Pain had been the outstanding symptom from the moment of injury. It started within two minutes and increased to such a peak in 2 to 3 hours that he begged to have the arm removed. The pain at first was located in the fingers, but in the next two hours spread to both the palm and the thumb. It was restricted to the palmar aspect and the hand was much swollen ; since then the pain had not changed though he thought that he was getting accustomed to it, as at first he required much morphine. He had learned that keeping the hand absolutely still and avoiding excitement mitigated the pain. The pain was variously described as a crushing burning, and as though a burned area were being held in front of the fire. Sudden bursts of pain were indescribable. Factors altering the pain were various. The weather did not seem to affect it, but any noise, such as a slamming door or the sound of aeroplanes, was extraordinarily painful. Low-flying aeroplanes made him nervous, and he could not say whether this was because of the pain or for some other reason. Thus he had become accustomed to flinch whenever a fast-moving truck went by, but when this occurred while his sympathetic chain was blocked he was at a loss to understand why he flinched until he remembered that he usually had pain at such times. When asked about the cinema he said he never went, and in explanation he described how he had gone to see the Marx Brothers in " Big Store " and found that the scenes of singing and dancing gave him pleasure, but when a mad chase on bicycles and roller skates was portrayed, he had to close his eyes to try to escape the pain that the excitement produced. The only time that he was really free from pain was if he should chance to wake up very slowly and then his hand would be quite painless until he was disturbed. The pain was made worse by putting the hand in warm water and somewhat relieved by putting it in cold. He considered that the hand was unusually dry, and so kept it covered with a moist cloth and felt more comfortable this way, though at first even the water was unbearable and he used vaseline.

Examination, which was difficult, revealed partial lesions of the median and ulnar nerves, as shown by moderate power in the long flexors of the wrist and fingers, but absent power in the long flexor of the thumb and of all the intrinsic muscles. Appreciation of light touch and pin prick was lost in the distribution of the median nerve, but was present in that of the ulnar. The patient said that this had but recently returned. Apprehension was so great that at first there appeared to be hyperæsthesia of the whole hand, any approach to it causing withdrawal with expressions of pain. Later, however, when confidence was gained it was found that when the eyes were shut neither light touch, pin prick, nor heavy pressure could be felt on the index finger, though when the eyes were open these caused great pain. He was able to touch the hand much more freely than he would allow others to do.

He stated that the fingers were always warm and pink, and two experiments recording skin temperatures for 45 minutes showed that the blood-flow to the little finger was always much greater than that to the normal contralateral fingers, while the flow to the index finger was variable (Fig. 4, Exp. 1 and 2). The skin of the palm was thin and atrophic. The median area was anhydrotic, while the ulnar area sweated, but not excessively.

X-rays on admission and three months later showed a progressive decalcification of the Sudeck type (Fig. 5).

Other investigations showed:—

1. Block of all the nerves at the wrist did not reduce the pain, but in some way altered its character.
2. Block of the sympathetic chain gave complete relief (Fig. 4, Exp. 3).
3. No relief was experienced by a course of X-ray treatment to the hand, while a similar course of treatment direct to the nerve trunk at the sight of the lesion likewise caused no change in the pain.

Sympathectomy was therefore advised, and in the seventh month an operation was performed by the posterior approach and a segment of what appeared to be the sympathetic chain was removed. Inasmuch as all concerned were convinced of this it was somewhat disconcerting to find that the patient was only partially

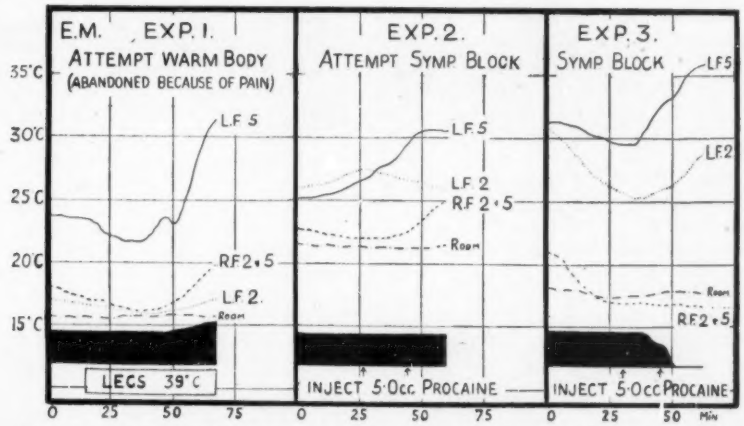

FIG. 4.—Temperature charts of subject E. M. Conventions as in Fig. 2.

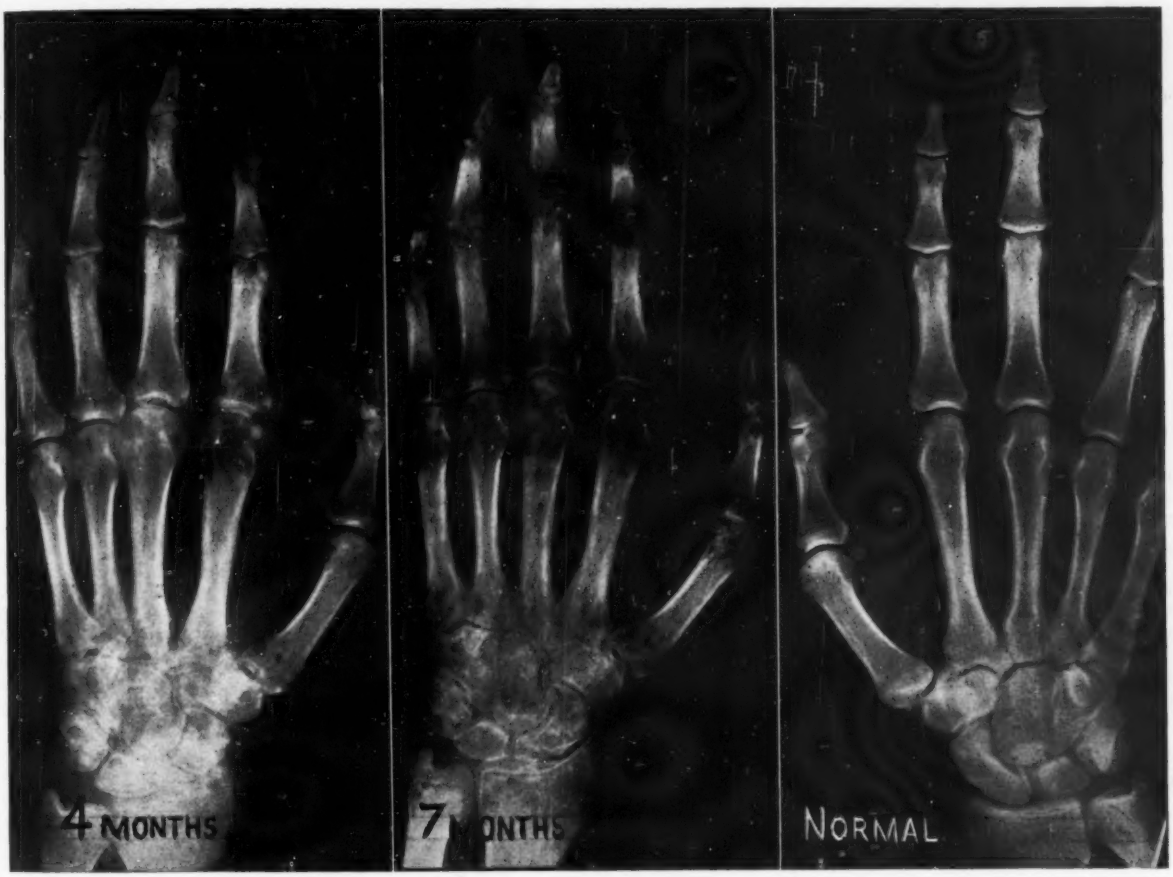

FIG. 5.—X-rays of subject E. M. taken 4 and 7 months after injury. The normal right hand shown at the right was taken at the same exposure as the left hand at 4 months.

relieved for 2 to 3 days and thereafter suffered his usual torments. Clinical opinion at this time wavered between calling the patient a hysteric and deriding the method of therapy. These points are mentioned to stress the fact that operation plus other forms of strong suggestion did not avail to convince him that he had no pain. It was then found that sweat was present on the face and arm of the operated side, and histological section of the excised nerve showed no ganglion cells. One month later the patient submitted to a sympathectomy by the anterior approach, and thereafter was free from pain.

At the second operation (by anterior approach) location of the stellate ganglion was exceedingly difficult owing to scarring following the previous operation. A large nerve filament was found which joined the first dorsal root in front of the first rib. It appeared to come up from the second or third root of the sympathetic trunk. This, together with a large fragment of tissue in the position of the stellate ganglion was resected. Histologically many ganglion cells were present in the section.

On regaining consciousness the patient volunteered that he was free from pain. His temperament underwent a great change. He became cheerful, very interested in his surroundings, and made several fast friends in the ward. He developed into a habitué of movie shows and concerts, and was unaffected by noises, excitement, or other stimuli. His hand remained dry and warm and the range of movement in his fingers increased, so that he was able to write clearly. He used the limb almost normally, and was recently seen in the ward carelessly brushing back his hair with the formerly causalgic hand.

F. L., aged 33. *A Case of the Proximal (?) Causalgic Syndrome.*

Admitted four months after receiving gun-shot wounds (shell-fragments) of the left shoulder and anticubital space. He sustained a compound fracture of humerus with what appeared to be a complete ulnar and median palsy.

One month after injury following remanipulation of left humerus he noticed severe pain in left hand. He described the pain as " terrific," but could not specify its quality. It was made worse by smoking, by the noise of aeroplanes and the wireless and by jarring of his bed. He lay in bed with knees drawn up and noticed severe exacerbations when these were straightened. Stroking the feet or other contact made the pain almost unbearable. He was irritable, solitary, and always depressed ; his manner almost cringing. The pain was felt diffusely on the palmar aspect of the hand including the anæsthetic ulnar area. It had become progressively worse since the injury. Analgesic drugs failed to give relief, even in large doses and only morphia secured for the patient a few hours sleep. Otherwise the only relief he obtained was by holding a cold wet cloth in his normal hand.

The arm and forearm were œdematous and touching them increased the pain. The fingers and wrist were so stiff as to appear ankylosed. The skin on the dorsum was thin and shiny but on the palmar surface was encrusted and macerated owing to the impossibility of cleaning it.

In so far as clinical examination could be conducted it was evident that the patient had a complete ulnar and musculospiral palsy. There was definite diminution in appreciation of light touch and pin-prick in the median area with paralysis of the thenar muscles, but there was still some contraction of the long finger flexors supplied by the median nerve.

Stellate block at the fifth month with 2 per cent. procaine produced almost complete relief of pain temporarily.

Operation was delayed to the seventh month owing to condition of the wounds. Stellate ganglionectomy was then performed. Following this the patient had complete relief from his " terrific " pain, there remaining only a slight ache in the palm which the patient attributed to stiffness. The limb could now be handled without producing pain and other stimuli previously mentioned were without effect. He could smoke without pain and was able to discard his damp rag. He smiled when in conversation and was, in fact, a normal person. His fingers, of course, remained stiff, but it was now possible to initiate treatment.

A. B., aged 24. *A Case of the Distal Causalgic Syndrome.*

Admitted eight months after receiving a machine-gun bullet through the left upper arm, which fractured the humerus. The wound healed after only slight sepsis and the fracture united in normal fashion.

The day following the injury the hand became painful but was not swollen. The pain was situated on the palmar aspect of the hand, including the fingers and thumb and was also felt under the nails. It was extremely severe at first so that he required morphine and stated that he was " only able to live by sleeping most of the time." The pain was now tolerable, but he was not sure if this was only because he was accustomed to it. The pain was burning in character as though the hand were held in front of the fire and he could not pull it away. It was made worse by various things, but chiefly by excitement. He stated that thunder and lightning caused intense spasms of pain, and any sudden noise or seeing other patients quarrelling caused exacerbations of the pain. He was able to get relief by lying still in a quiet place. It was also eased to a certain extent by cold weather. It was made worse by anything touching the soles of his feet, as when putting his socks on, and it was also worse when he touched anything with his normal hand when it was dry, and he therefore preferred to keep this hand moist. He spontaneously remarked that drawing deeply on a cigarette caused the pain to be worse, and this also occurred when he was asked to take a deep breath.

Examination showed moderate weakness of all the muscles supplied by the ulnar and median nerves and no loss of sensation. Pin prick was felt as very unpleasant and seemed to increase the pain, while light touch was not disagreeable unless drawn across the skin. Deep pressure was painful, but the pain passed off if it was continued. The pain felt in the hand when other parts of the body were stimulated seemed to occur without delay. The pain was not diminished, but rather seemed to be increased by suprasystolic compression of the forearm.

He had noticed that the fingers had always been warm and pink and this condition was still present (Fig. 6, Exp. 1). The skin was thin but not sufficiently tight to be called glossy. There was marked atrophy of the finger tips and curvature of the nails. Sweating was profuse on the tips of the fingers and dorsum of the hand. A severe hyperextension deformity of the metacarpo-phalangeal joints was present.

X-rays showed marked decalcification probably of the Sudeck type (Fig. 7).

Block of the sympathetic trunk caused complete relief of all pain (Fig. 6, Exp. 2). Block of the ulnar and median nerves in succession caused relief of pain in their respective areas, and this relief applied to the induced exacerbations as well as the spontaneous varieties of pain.

A series of X-ray treatments to the hand resulted in no improvement.

Stellate ganglionectomy was performed by anterior

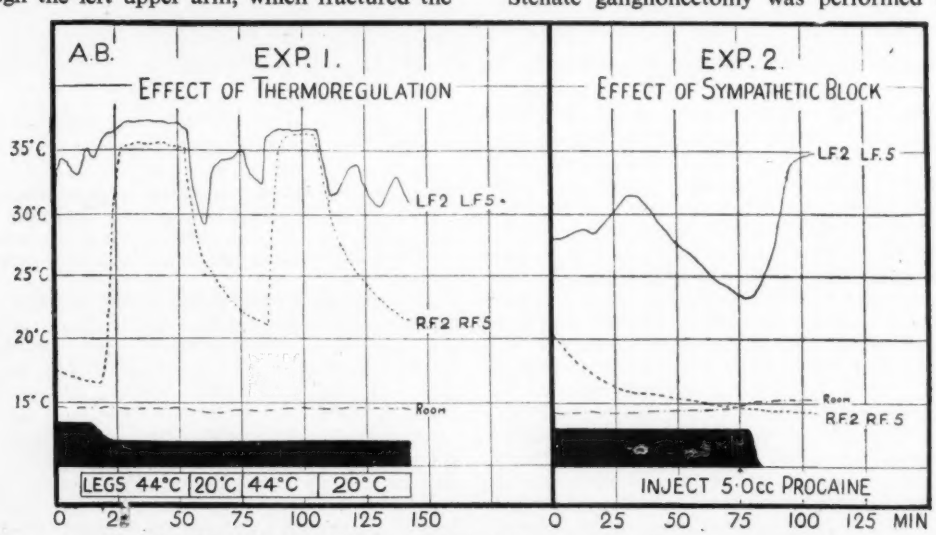

FIG. 6.—Temperature charts of subject A. B. Conventions as in Fig. 2.

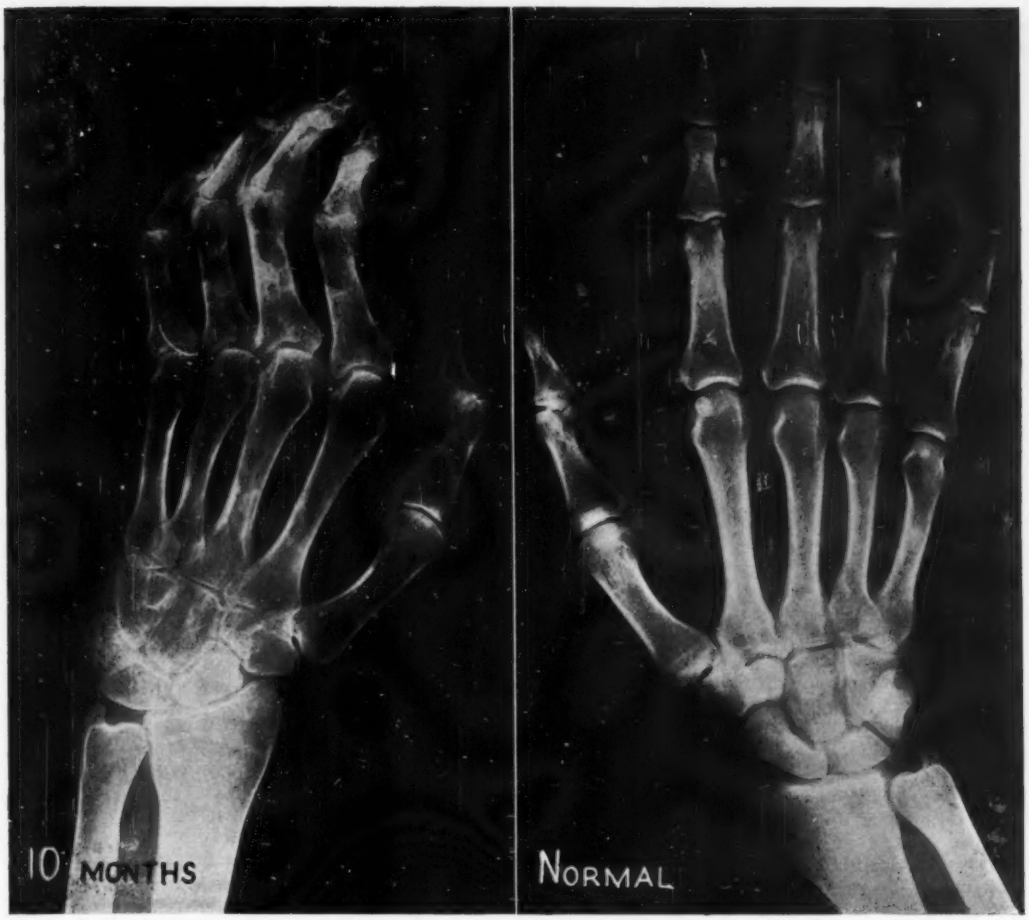

FIG. 7.—X-rays of subject A. B. taken 10 months after injury. The hands were simultaneously exposed.

approach in the fourteenth month. Following resection of the ganglion the patient developed a well-marked Horner's syndrome which for a few weeks was rather troublesome. Spontaneous pain completely disappeared after operation, and he was well able to tolerate active measures to correct the deformity. Sensation to light touch and pin-prick was normal in all areas except that there was slight paræsthesia in the median distribution.

M. S., aged 24. *A Case of the Distal Causalgic Syndrome.*

Six months before admission he received a machine-gun bullet through the soft tissues of the right arm 2 in. above the elbow. Healing of the wound occurred without infection.

Three days later pain commenced when he awoke from an anæsthetic during which the arm had been put in plaster. Within 24 hours it had become intolerable and he received morphine for relief. Since then it had become much less, but was still very uncomfortable. The pain had always been situated chiefly in the palmar aspect of the middle and ring fingers and adjoining part of the palm. Since its onset it had been of a severe aching character which he could not describe. It was increased by a variety of things, such as noise, swallowing, taking a deep breath, going to a concert, and seeing people fight. He also said that gripping with the good hand caused the pain, unless he gripped on a damp rag. The pain was worse in hot weather than in cold.

Examination showed a slight weakness of the muscles innervated by the ulnar nerve with a complete loss of sensation in the ulnar area. There was a hyper-reaction to light touches in the median nerve area, and such stimuli increased the pain.

The condition of the hand was not obviously different from that of an ordinary ulnar nerve palsy, except that the skin of the median area was thin and showed the effects of lack of use. Temperature records for a period of 2 hours were not obviously different from those of an ordinary ulnar nerve lesion (Fig. 8, Exp. 1). Sweating

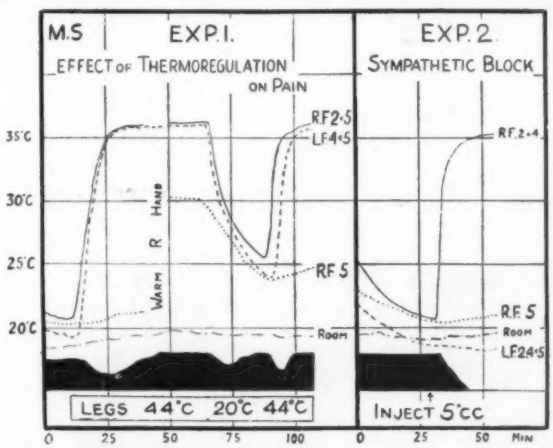

FIG. 8.—Temperature charts of subject M. S. Conventions as in Fig. 2.

was slightly more profuse in the median area than in the normal and was absent in the ulnar area.

X-rays showed decalcification of indefinite type.

Sympathetic block caused complete relief of pain (Fig. 8, Exp. 2).

Block of the ulnar nerve at the wrist caused no change in the hand except a palsy of the ulnar innervated muscle. Block of the median at the wrist caused complete relief of all pain and discomfort.

X-ray treatment to the median nerve at the level of the lesion caused no relief except some tenderness in this region was abolished. Two weeks later a further course of treatment was given to the hand with no benefit.

In the eighth month the nerves were explored. The median appeared normal, while the ulnar was almost completely divided. Resection and suture of the ulnar was performed and the nerves placed in a fresh bed. He was free from pain for four days, but then the pain returned with greater intensity than ever.

One month later repeat block of the stellate ganglion with 2 per cent. procaine (10 c.c.) gave complete relief of pain. The hyperæsthesia and tenderness of the palm were also relieved.

In the ninth month stellate ganglionectomy by the anterior approach with resection of the second ganglion produced a mild Horner's syndrome. Since operation the patient has been absolutely free of pain and the hyperæsthesia has not returned. He now has a full range of movement in his fingers and use of the hand is limited only by the ulnar nerve lesion.

W. A., aged 25. *A Case of the Distal Causalgic Syndrome.*

Three days before admission he was accidentally shot through the right axilla. Immediate operation had disclosed that the axillary vein was divided and this was ligatured; the artery was intact. The condition of the nerves was not determined.

On admission he complained of a throbbing pain in the wound and there appeared to be a complete block of the median, ulnar and musculospiral nerves. One week after the injury he began to have an aching pain down the ulnar side of the forearm extending into the palm of the hand. This was fairly constant, but at times would disappear for a few minutes, and it was sufficiently severe to prevent more than two or three hours sleep. This pain disappeared in the course of two to three weeks. About six weeks following injury, the sensation began to return to the median and musculospiral areas, with a concomitant return of muscular power. No sign of function was found in the ulnar nerve. At this time the patient began to complain of a burning searing pain in the part of the hand to which sensation had returned. This pain was very severe, and its depressing effect was very apparent on the face of the patient, which became haggard and careworn. The pain was aggravated by any attempt to move the hand or wrist and by even the lightest touch over the median nerve. It was relieved by keeping as quiet as possible and avoiding excitement. When asked about the cinema he reported that he had to close his eyes during the action scenes in order to lessen the pain. At this time slight hyperhydrosis of the median area was present and because of the fixed position of the hand the skin was macerated and did not present the appearance of " glossy fingers." There was moderate œdema and limitation of movement at all the joints.

X-rays showed marked evidence of Sudeck's atrophy (Fig. 9).

At the third month after injury there being no signs of improvement in the pain nor any return of function to the ulnar nerve, the brachial plexus was explored by Mr. R. Barnes. The median nerve appeared normal and was only involved in the thinnest scar tissue. The ulnar nerve was found divided and required suture. The axillary vein was represented by a fibrosed cord while the artery appeared normal. A peri-arterial sympathectomy was performed by stripping the adventitia off the vessel for a distance of 5 cm.

After operation the pain was diminished for approximately one week and then returned to its former intensity, still being felt only in the median area.

The sympathetic chain was blocked twice in the fifth month with good, but only temporary, relief. Block of the median nerve at the wrist abolished all pain in the hand.

A series of X-ray treatments was given to the hand in the sixth month and approximately 7 to 10 days later he began to improve. In the ensuing two weeks further improvement occurred so that though he was not free from pain, he looked less careworn and the hand could be handled much more freely. Improvement thereafter was continuous though slow, and there remained much pain on attempting to move the stiff joints. At the end of the twelfth month he was sufficiently recovered to be able to return to his work as a shoemaker, but still experienced slight pain associated with emotional excitement. When last seen at the twenty-fourth month, all the muscles innervated by the ulnar nerve were contracting, there was only a vestige of pain, though still considerable limitation of joint movement and the X-rays show recalcification of the porotic bones.

W. E., aged 32. *A Case of the Proximal Causalgic Syndrome in a Phantom Limb.*

One year before admission the patient was wounded in action and disarticulation of the right arm at the shoulder was performed 24 hours later. He also sustained compound fractures third, fourth, and fifth fingers of the left hand.

Two to three weeks after injury pain began to be felt in the phantom right hand. This was a tight sensation at the base of the thumb and a severe searing sensation in the ring finger, though the whole hand was affected to a moderate degree. There had been little change in it since it first developed. The pain was nearly constant, but was greatly aggravated by any excitement. As an illustration he told how the pain became almost unbearable if when the train in which he was riding suddenly passed another going in the opposite direction. It was also ascertained that a sudden noise made experimentally caused a marked increase in the pain. It was found that a deep breath caused a momentary exacerbation of the pain.

Examination showed the stump to be in good condition and the scar well healed. In one place, however, on the anterior aspect pressure on the scar caused a pain to shoot down the phantom limb and at the same time the pain in the hand became worse.

Experimental procedures were necessarily restricted to observing the effect of procaine block of the stellate ganglion. This produced complete relief of pain, which preceded the development of a Horner's syndrome by several minutes. This procedure was repeated on three occasions with only temporary relief. Circumstances beyond the patient's control prevented a sympathectomy being done.

R. D., aged 52. *A Case of Dystrophic Pain.*

Three weeks before admission was wounded in the right axilla by a bomb splinter. At immediate operation the median nerve was found frayed, the ulnar nerve was divided, and it was sutured, while the brachial artery and vein had lateral holes. These vessels were divided and ligated.

Pain commenced when he recovered from the anæsthetic and had been present ever since as a severe aching in the distribution of the median nerve. It was a constant crushing sensation, made worse by letting the arm hang down or attempting to move the fingers and was also worse at night. It was not affected by emotional stress, loud noises, or other such stimuli. There was moderate swelling of the hand, reduced sweating and fixation of the joints. The œdema and joint affection were equally prominent in the ulnar distribution. Skin temperatures recorded at various times were not obviously different from those of an ordinary ulnar nerve lesion (Fig. 10), while oscillometric tracings from the forearms showed a greatly reduced pulsation on the affected side.

An exploration was performed by Mr. A. S. Kerr at the third month. The median nerve was found to be involved in slight scar tissue while the ulnar was the seat of a neuromatous formation, but regeneration appeared to be progressing. The brachial vessels could not be defined, and after neurolysis the wound was closed.

The condition remained unchanged until about the

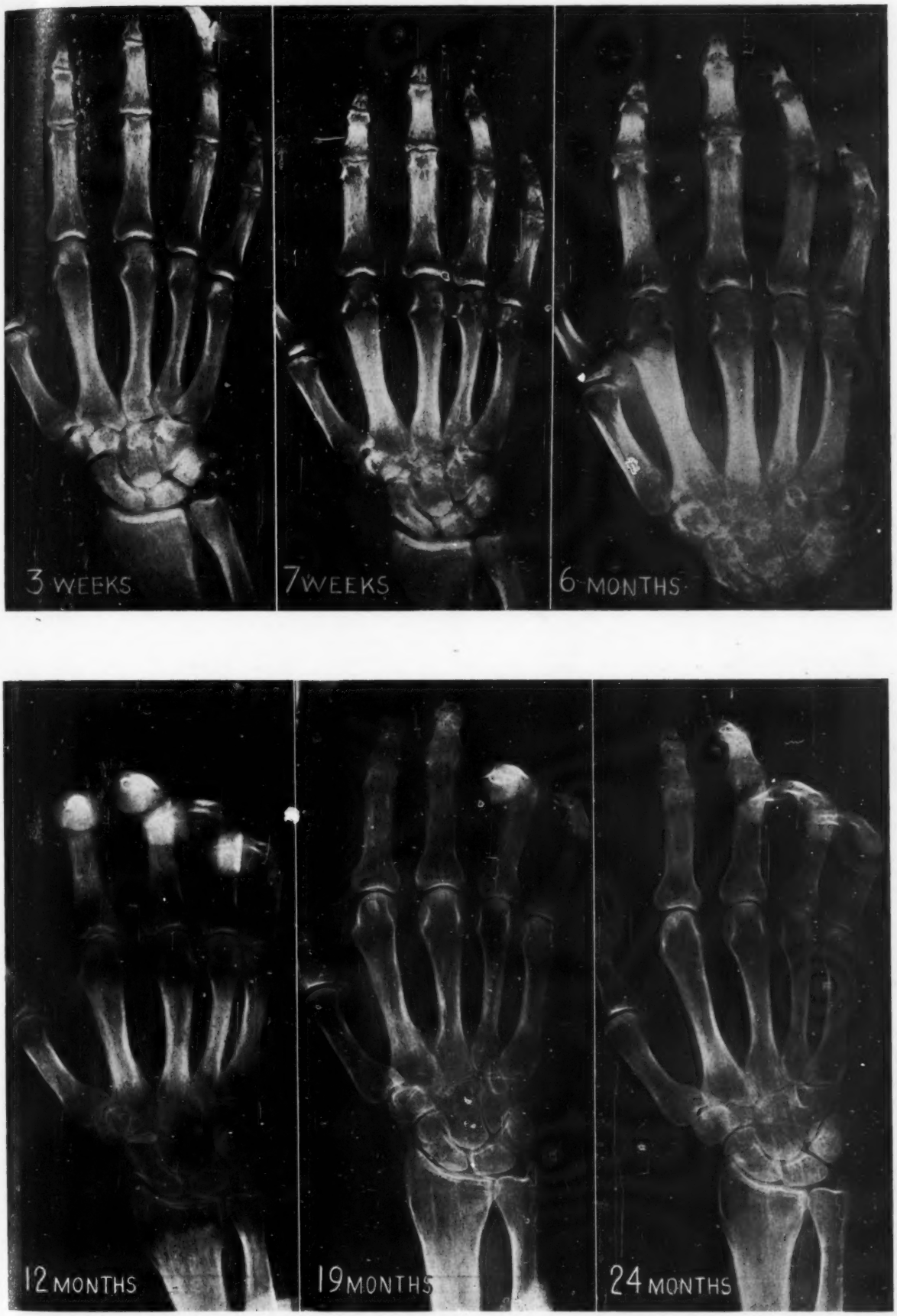

FIG. 9.—X-rays of subject W. A. taken at the times indicated after injury. That taken at the third week was in no way different from the normal exposed at the same time and not reproduced here.

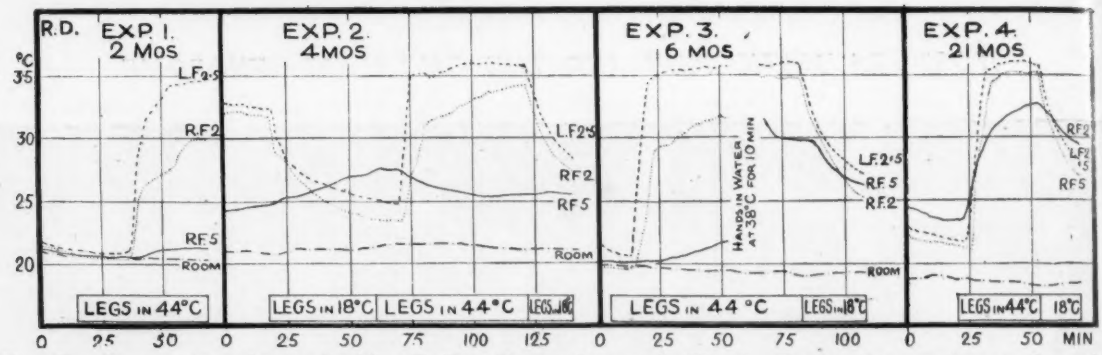

FIG. 10.—Temperature charts of subject R. D. Conventions as in Fig. 2. During the experiments the pain was slight and the patient's statements inconsistent.

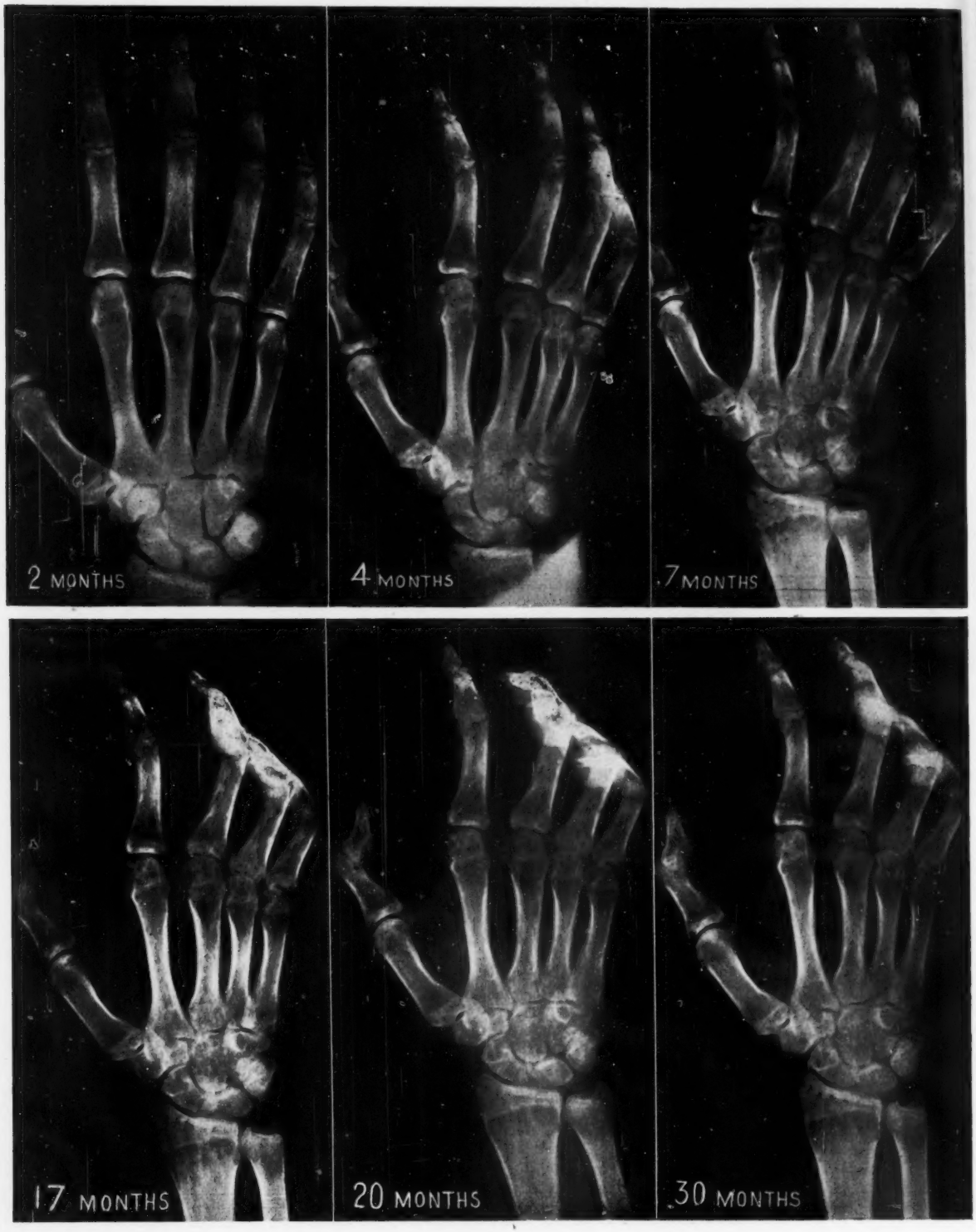

FIG. 11.—X-rays of subject R. D. taken at the times indicated after injury. That taken at 2 months was in no way different from the normal exposed at the same time and not reproduced.

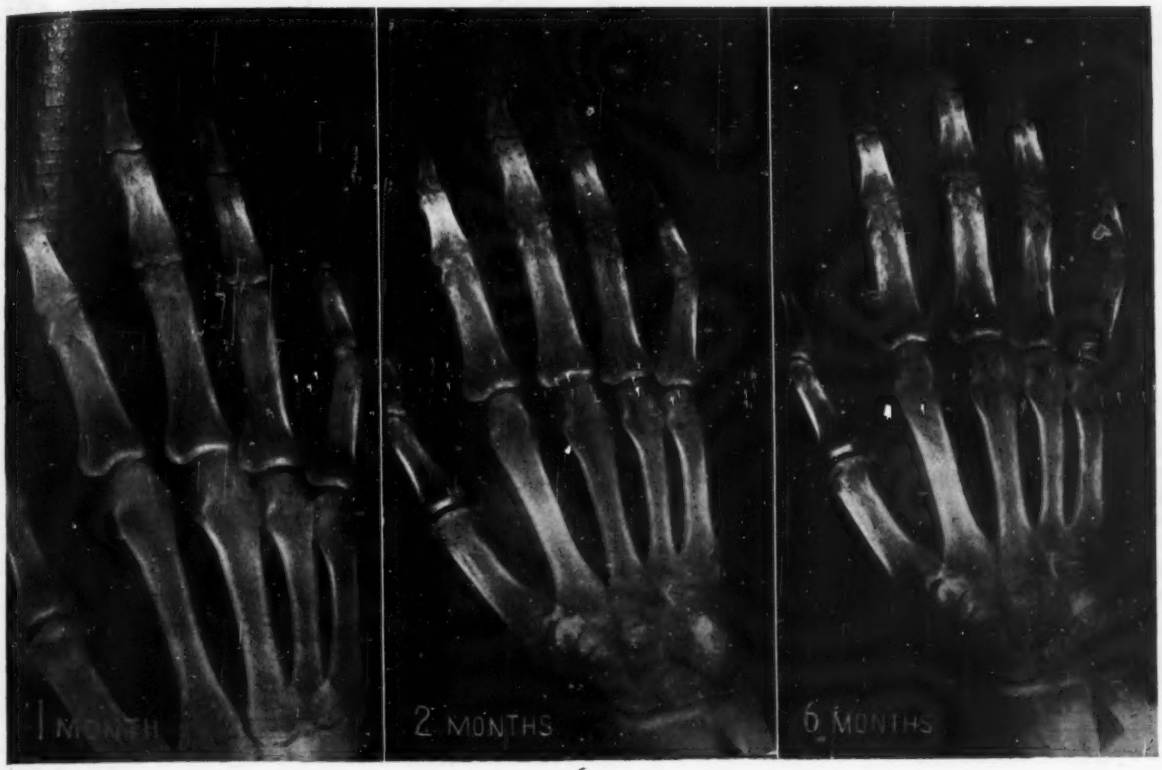

FIG. 12.—X-rays of subject W. C. taken at the times indicated. That taken at 1 month showed little difference from the normal exposed at the same time and not reproduced here.

fifth month, when pain began to get less. At this time the œdema had disappeared and the skin was very tense and shiny.

X-rays showed well-developed Sudeck's atrophy (Fig. 11).

A clue to the nature of this patient's disability was now obtained for he complained bitterly about the sensations aroused from the regenerating end of the ulnar nerve. These sensations seemed to loom as large in his consciousness as did the pains attributed to the dystrophic changes so that it became a matter for speculation as to whether he was not unduly pain susceptible.

W. C., aged 41. *A Case of Dystrophic Pain.*

One month before admission fell and fractured the right humerus, which was associated with a lesion of the musculospiral nerve.

Following the injury he said that he had moderate pain in the back of the hand for two weeks. This was usually noticed for 1 hour after he went to bed.

At the time of admission he complained of no spontaneous pain, but heavy pressure on the dorsum of the hand or full extension of the fingers was painful. The hand was moderately swollen and had been supported on a straight finger splint. The musculospiral nerve palsy was recovering. The further course was uneventful, except that at the fourth month he refractured the humerus and thus required further care in hospital. Physiotherapeutic treatment restored movement to the joints. In the next few months he occasionally complained of odd aching sensations in the hand and those were most in evidence at night.

X-ray showed definite osteoporotic decalcification of the carpus (Fig. 12).

F. B., aged 32. *A Case of Dystrophic Pain.*

Three months before admission he sustained a fracture of the right tibia and fibula, which was treated in plaster-of-paris.

On admission the plaster was removed and the fracture appeared firmly united. On attempting to commence weight bearing the patient complained of an aching pain in the foot. There was no obvious limitation of movement and no tenderness on pressure, but X-rays showed a definite spotty decalcification (Fig. 13).

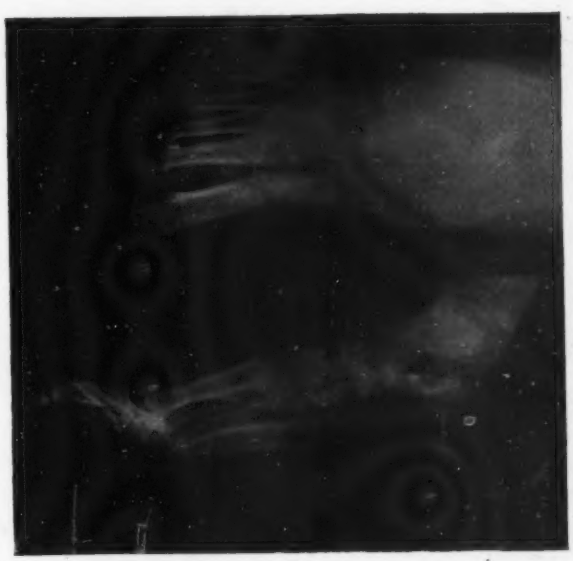

FIG. 13.—X-ray of subject F. B. 3 months after injury.

In the course of the next month the pain diminished and only recurred on walking long distances.

R. L., aged 31. *A Case of Psychogenic Pain.*

Six months before admission he sustained multiple wounds of the back of the right thigh by fragments from an explosive cannon shell.

He stated that 4 to 5 days after the injury he began to have a severe aching pain in the right foot, which prevented sleep for two months. It was steady in character, comparable to a toothache, and was situated on the dorsum of the foot. He knew of nothing that relieved it, though radiant heat made it worse. He had received ionization treatment to the scars on the thigh without benefit. This pain had persisted and was severe, but did not prevent him walking, but it prevented him doing physical training. It was worse at night when trying to get to sleep, but was less noticeable when at the cinema.

Examination showed no abnormality of the foot. The pulses were equal and there was no limitation of movement, nor was there any disturbance of sensation. There were many metallic foreign bodies in the thigh, but they were not associated with any tenderness.

X-rays of the feet showed no rarefaction.

He was at first accepted as being quite genuine and in this spirit preparations were made to test the effect of lumbar sympathetic block. Shortly after the insertion of the needle and before the injection of the anæsthetic, he became free of pain for the first time since injury. However, in another two to three minutes the foot became numb and useless, in particular he noticed that he could not flex his toes. Nevertheless, a well-marked flexor response to plantar stimulation was easily obtained. It now became quite clear that this was a case of hysteria and he was told that the numbness would pass off in 2 to 3 hours and he would thenceforth be free of pain. The following day he was free of pain, but complained of tingling feelings when walking.

D. P., aged 25. A Case of Osteoporosis and Hyperhydrosis without Pain.

Ten months before admission he received a wound from a machine-gun bullet causing a compound fracture of the lower end of the radius and the ulna and a median nerve injury of the right arm.

On admission he was found to have chronic osteomyelitis of the radius with non-union of the fractures, marked osteoporotic changes in the bones below the level of the lesion (Fig. 14) and a complete lesion of the median and radial nerves. The condition of the index and middle finger qualified for the description of glossy fingers. The skin was thin and tight so that all the creasings and markings were nearly obliterated. The nails were extraordinarily curved and thickened, and the digits were tapered almost to a point. The temperature of the two sides of the hand varied, but usually the median nerve area was cold; sweating in the ulnar area was excessive but was absent in the median and radial areas. At intervals of some months crops of vesicles would appear on the hand irrespective of the nerve distribution and in the ulnar areas they caused an itchy sensation.

Despite all the objective signs of causalgia this patient had no pain.

The subsequent course was not noteworthy. Under appropriate treatment the osteomyelitis was cured and the fracture healed. Otherwise at the end of 30 months there was little change, the hand being of use only to steady light objects.

Discussion

In commenting on these patients it is helpful to consider that post-traumatic pains may be produced by several different mechanisms. On this basis the pains may be divided into three groups: (1) psychogenic, (2) causalgic, and (3) dystrophic. The significance of the first two terms is self-evident, while the term dystrophic has been selected, not because it is non-committal, but because it seems to express the view that the pain is secondary to a disturbance of nutrition in the extremity. A brief note may be ventured on each of these three types without attempting exhaustive discussion.

FIG. 14.—X-rays of subject D. P. taken at the times indicated after injury. The normal left hand was exposed at the same time as the right at 14 months.

1. *Psychogenic.*—Case R. L. suffered from pain of this type as shown by the therapeutic efficacy of a mock attempt to block the sympathetic chain. There was also other evidence of the liability of this patient to develop hysterical manifestations. Such cases were easily distinguishable from those of the causalgic syndrome, but failing the aid of the therapeutic test they might well have been confused with the dystrophic group. This particular patient, however, showed no sign of trophic disturbance, but if such had developed due to disuse as has been shown possible by Hurst (1940) the diagnosis would have been difficult. In fact it is not unreasonable to suppose that genuine dystrophic pain might supervene under these circumstances.

2. *Causalgic.*—This group consists of cases T. P., E. M., F. L., A. B., M. S., W. A., W. E., and H. G., whose pains were essentially of the one type, and this conformed to that described above as causalgic. Moreover, it is apparent that two groups of patients with the causalgic syndrome may be distinguished depending on whether the pain originates at a proximal or distal site as determined by peripheral nerve block. Thus for fuller diagnosis the term causalgic syndrome should be modified by either the adjective proximal or distal to denote the site of cross-stimulation. For complete diagnosis further enquiry will be necessary so that the conditions predisposing to the linkage of the sympathetic and sensory fibres may be stated. Of these it is not unlikely that vasospasm and ischæmia may play a part, a consideration which would explain the relatively high incidence of causalgic pain in injuries involving the root of the limb.

Attention should be drawn to the fact that many of the cases described here were not seen until several months after injury. Therefore, the descriptions of the initial symptoms depend on the memories of a period confused by fatigue, shock, and narcotics and may not be entirely reliable. However, taken at their face value they suggest that in the initial stages the severity of the pain may be too disconcerting for the patient to recognize the various features which characterize causalgic pain.

3. *Dystrophic Pain.*—Cases R. D., W. C., and F. B. exhibited pain of this type, which was typically of a dull aching character made worse by movement of the part and, in common with osteoarthritic pains, tended to be most in evidence at night. It is tentatively suggested that this pain is secondary to disturbance of nutrition consequent on any of the factors disturbing the environment of the tissues. These factors will include disuse, defective arterial supply, defective venous drainage, and defective lymphatic drainage. To imagine that there is also some individual predisposing factor to the development of dystrophic changes need not unduly strain the hypothesis; witness the wide range of subclinical peripheral circulatory disorders such as postural œdema, mild vaso-spastic states, and mild erythrocynosis; witness also the possibilities of individual variations in the buffering capacity of the blood and tissue fluids which would modify the nutritional changes. This conception of the varied factors causing dystrophic changes seems not only to be in accord with the facts, but in agreement with the views of Gordon (1934) and Frutiger (1939). It obviates the necessity of searching in these cases for some common factor, such as vasospasm or vasodilatation. It is not out of place to remark that the researches of de Takats (1943) on patients who apparently fall into this group, show that there is a tendency to an increased blood-flow in the affected extremities, but it yet remains to be shown whether this is a cause or an effect or merely a coincidental phenomenon such as would result from a slight interference with the vasoconstrictor nerves.

If such a view of the development of dystrophic changes which are characterized by œdema, bone resorption, and periarticular fibrosis be correct, it is easy to assume that these changes might give rise to pain. This pain, moreover, would likely be of the type described by these patients.

One puzzling feature which presents itself is the great disparity in the severity of the pain complained of by different patients. For this two explanations which are not mutually exclusive may be advanced. In the first place there may be in some cases an element of peripheral neuropathy, secondary to the nutritional disturbance of the limb, giving rise to dysæsthesia distorting the ache into an agonizing pain. Evidence for this might be found in the disturbances of cutaneous sensation which are frequently described. In the second place there is good reason to believe that there is much psychogenic exaggeration of the pain in the most severe cases. Here the analogy to cases of post-traumatic headache is too close to be lightly dismissed. Not only is the hand of similar emotional significance as the head but the two types of case are similar in age incidence, frequency of compensation proceedings, and in their response to a variety of therapies in the hands of different proponents. In regard to the latter reference may be made to treatment by periarterial sympathectomy (Herrmann and Caldwell, 1941), X-ray (Mumford, 1938), physiotherapy (Henderson, 1936), carbaminoylcholine ionization (Middleton, 1937), alcohol injection of nerves (Turner, 1936; Little, 1939), and typhoid injection (Cravener, 1936). It is not the intention to impugn any one of these modes of therapy, but to endeavour to show that as in a case of chronic post-traumatic headache, so in one of post-traumatic dystrophic pain there is not only some cause to doubt the organic basis of a disabling symptom, but also leeway for major differences of opinion between clinicians.

In conclusion, it may be said that a diagnosis of dystrophic pain should include not only an assessment of the psychogenic element, but also an indication of the factors responsible for the dystrophy. One may hope that such an ideal may soon be attainable.

Summary

It was noted that there was a need for a clearer definition of post-traumatic pain.

An attempt has been made to define the causalgic syndrome, using as a basis a theory of the mechanism of production of the symptoms.

This theory ascribed the peculiar qualities of causalgic pain to stimulation of sensory fibres by efferent impulses in the sympathetic fibres.

Evidence in favour of such a linkage was obtained from a study of the reactions to a variety of stimuli and from the results of peripheral nerve, nerve root, and sympathetic chain block.

Two types of causalgic syndrome were described depending on whether the site of conjunction of the sympathetic and sensory fibres was proximal, i.e. at the site of the nerve lesion or distal, i.e. near the terminations of the fibres.

It was considered possible that the distal type could occur as a result of some disturbance of metabolism due to œdema, ischæmia, or some other factor determined by injury to the limb as opposed to a primary injury to the nerve trunk.

A series of cases exhibiting post-traumatic pains was reported, and these were grouped under the terms psychogenic, causalgic, and dystrophic.

Comment was made on the vascular and nutritional changes with particular reference to osteoporosis. This reaction was considered to be non-specific, and it was shown to occur independently of the peripheral nervous system.

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A HEURISTIC THEORY OF NEUROSIS*

BY

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(RECEIVED 15TH MAY, 1944)

Introduction

IN a recent communication (Slater, 1943), based on a statistical survey of two thousand neurotic soldiers, a hypothesis was developed to the effect that there was a generalized predisposition towards neurosis, which was in large part responsible for the appearance of neurotic symptoms in the individual when placed under stress. Evidence was adduced that this constitutional tendency, though it might be affected by such environmental factors as early processes of conditioning, was, at least in part, dependent on hereditary factors. Evidence was also brought that it could usefully be considered in a quantitative manner, and that so considered the intensity of the constitutional predisposition varied inversely with the degree of stress under which the individual was placed before breakdown occurred, i.e. the greater the intensity of the constitutional predisposition, the less was the degree of stress required to produce breakdown, and *vice versa*.

On this last point, strong confirmatory evidence has recently been supplied by Symonds (1943). He states " the incidence of neurosis in different tactical duties varies directly with the amount of hazard encountered, as measured by the casualty rates." He also provides a table correlating the degree of predisposition with the degree of stress in 2,200 neurotic casualties, which shows that the degree of flying stress falls steadily as predisposition increases. From his table a correlation coefficient between the two variables of $-0{\cdot}26 \pm 0{\cdot}02$ can be calculated.

In the paper referred to no very detailed analysis of the nature of the neurotic predisposition was undertaken. Yet the frequency of various traits of personality was shown to vary significantly in the several diagnostic groups, and significant and fairly high correlations were found between personality traits and eventual symptomatology. There was, therefore, evidence of constitutional heterogeneity in the population investigated. On the other hand all the neurotic personality traits were noted as being at least sometimes present in all the diagnostic groups, and the same was true of all the classes of symptoms observed, with the exception of obsessional compulsive symptoms and psychotic and organic symptoms. This means in effect that the different neurotic groups fade off into one another clinically, and do not form qualitatively distinct groups. This observation is one with which every clinician is in practice familiar.

This, then, is the starting point of the argument which is developed in the following pages. It is our purpose to reduce the hypothesis already propounded to precise terms which may be handled statistically, and made the basis of predictions which can be checked by further observations. What is involved is, in fact, a general theory of the nature of the neurotic constitution.

Possible Theories

The various theories which may be advanced to account for the phenomena of the neuroses seem capable of being divided into three classes. By the first of these, neurotic phenomena are regarded as a type of response to which all human beings are equally liable, such as, for instance, the general tendency to respond with fever to the occurrence of an infection. Differences between individuals would then be related solely, or at least to a preponderant extent, to environmental effects. This theory has been very commonly, even if implicitly, held in the past; but it has of late been found inadequate. If this were an adequate explanation of the phenomena we have to discuss we would expect, as indeed we find, that the intensity of the stress under which an individual was placed would be directly related to the frequency of nervous breakdown. But we would in addition expect to find a direct relationship, both qualitative and quantitative, between the type and intensity of the stress and the type and severity of the breakdown. This is true only to the most limited extent. In the survey referred to there was evidence that the terrifying stresses of war tended to provoke anxiety states to a significantly preferential extent, but they did so far from regularly. A more important determinant of the type of response was the constitution of the individual as shown by his family history, previous life, and personality. This theory, in fact, breaks down by not taking into account or explaining in any way the very large amount of evidence of the existence of constitutional differences between individuals in these respects, and especially of their genetic aspects. It would leave

* Based on a paper read before the Genetical Society on 6/1/44.

unexplained the results of investigations of personality differences and similarities in binovular and uniovular twins (Kranz, 1936; Lange, 1929; Newman, Freeman, and Holzinger, 1937; Stumpfl, 1936, etc.), and the evidence of the familial incidence of neuroses and psychopathy (von Baeyer, 1935; Berlit, 1931; Brown, 1942; Brugger, 1935; Curran and Mallinson, 1940; Gebbing, 1932; Kolle, 1932; Kraulis, 1931; Lewis, 1936; Pohlisch, 1934; Riedel, 1937; Ritter, 1937; Schröder, 1939; Slater, 1943, etc.). In so far as early environmental differences might help to explain individual differences in disposition in later life, one would expect to find an association between the occurrence of neurosis and place in order of birth; the evidence is against this (Brown, 1942; Slater, E., 1944). This theory must be rejected.

The second theory that engages our attention is that the neurotic constitution is of a unitary kind, but dependent on genetic factors. It is possible to consider this theory in two forms. By the first, the genetic basis would lie in a single abnormal gene, whose variations in expression could be accounted for by environmental differences and by differences in genetic modifying factors, the so-called genotypic milieu. Theories of this type provide a sufficient account of the relevant data in such psychiatric conditions as phenylpyruvic amentia (Jervis, 1939), juvenile amaurotic idiocy (Sjögren, 1931; Jervis, 1941), gargoylism (Halperin and Curtis, 1942), oxycephaly (Ferriman, 1941), epiloia (Gunther and Penrose, 1935), Huntington's chorea (Sjögren, 1935), cerebral dysrhythmia and epilepsy (Lennox, Gibbs, and Gibbs, 1939, 1940, 1942), manic-depressive psychoses (Kallmann, 1941; Slater, 1936, 1938), schizophrenia (Kallmann, 1938; Kallmann, 1941; Koller, 1939; Lenz, 1937; Luxenburger, 1937; Patzig, 1937, etc.). In all these conditions findings are made which are believed to be specific for the condition in question; and it is worth remarking that similar investigations of neurosis and psychopathy have not resulted in comparable findings. On the basis of the theory, transitional forms between the normal and abnormal may occur, but will either be relatively infrequent, or will be capable of resolution with more refined examination into character-bearers and normals. Where this is only doubtful, as, for instance, in manic-depressive psychosis, some doubt is thrown on the postulation of a single gene. If a single abnormal gene were postulated as the basis of neurosis, necessary consequences would be that neurotics would prove to be relatively homogeneous, and would show some highly discriminant characteristic which would differentiate them with fair certainty from the average population. As will later be shown, the evidence is against homogeneity, and no single discriminant characteristic has so far been discovered.

The alternative form of the second theory is that the neurotic predisposition, though still regarded as unitary, is dependent on a large number of separate genes of small but similar effect. This postulation would allow us to explain quantitative variation in the intensity of the neurotic predisposition, and would also permit the inclusion of neurotics within the limits of range of the general population. The outstanding example of a finding which is accounted for in this way is the distribution of intelligence in the general population. Fraser Roberts (1939), describing the situation, writes:

> "General intelligence, in this sense, is a graded character and displays continuous variation from one extreme to the other . . . Over the great bulk of the range there is no discontinuity . . . A frequency curve is found to conform to the normal form. But at the extreme ends of the distribution, most certainly at one end, we find variations which are no longer continuous, and the curve is no longer normal . . . Without discontinuity anywhere we pass from the brilliant to the superior, the average, the dull, the very backward, and finally to the mentally defective. At the very lowest levels, however, we find not merely the very backward; we find gross deviations, the idiots, and the imbeciles . . . This portion of the curve is far from normal, for such individuals are far too numerous. The distinction, on the basis of measurement only, is not absolute . . . (but) is fundamental genetically . . . We have, on the one hand, multifactor inheritance, on the other hand, the transmission of single genes; on the one hand, the genes of individually small effect, on the other, the gene whose bearer is sharply distinguished from the rest of his fellows . . . It is not impossible to mark approximately the line of division between the two types of mental defective. On the Binet scale it may be drawn roughly at an I.Q. of about 45 . . . Feeble-minded persons must be regarded as abnormal, but this is probably true only against the background of our present complex civilization. They are merely the extreme minus end of the normal distribution of intelligence."

This theory is still capable of explaining all the important genetic data on mental defect, and long occupied a prominent position in the field of psychometric psychology. Spearman and Hart (1912) put forward the view that all mental processes belonged to a single class, and that the interrelations of all tests used to measure them could be accounted for in terms of a single common factor, *g*. More recently, however, this theory has been shown to be inadequate, and even when only cognitive tests are used, most tables of results indicate the operation of more than one common factor. A continuous variation from brilliance to defect is found in adequately measurable cognitive abilities other than intelligence (such as spatial judgment), and frequency distributions are of the normal form. Methods of assessing variations in temperamental characteristics have not been carried far enough at present to provide critical evidence, but there is no reason to suppose that the frequency distributions depart from normal. Thus the distribution of psychological characteristics is currently supposed to be of the multivariate normal form.

A necessary consequence of the unitary theory is the homogeneity of selected samples. If adding and subtracting depend on the same ability, men who add equally well are not likely to differ greatly in ability to subtract. Similarly if the neurotic predisposition is a unitary trait, variations in characteristics which differentiate neurotics from normals will

be smaller among neurotics, who form a selected sample, than among an unselected normal population. The presence or absence of homogeneity among neurotic subjects is therefore a matter of crucial importance; if it fails to hold, as Roberts points out is the case in the lowest reaches of mental defect, the theory breaks down, and supplementary hypotheses have to be made.

But the heterogeneity of the neuroses is, actually, a commonplace of clinical experience. If it did not exist, we should not be tempted to diagnose one man as a hysteric, another as an anxiety neurotic, and a third as a depressive. In respect of purely qualitative findings the statistics already provided (Slater, 1943) may be relied on. Further data of a quantitative and therefore more precise kind will be adduced later on. It is sufficient to state here that the evidence on this point is, in our opinion, sufficient to render the unitary hypothesis of the neurotic constitution unlikely and not suitable for use as a weapon of research.

We come, therefore, to the third of the possible hypotheses of the nature of the neurotic constitution. By this theory the constitutional basis of neurosis is still held to be, in part at least, genetic in nature, but due to the operation of factors not all of similar effect. This theory again may be presented in two forms. In the first of these the several genetic factors would be supposed to be each in itself sufficient, at least under suitable environmental circumstances, for the production of a neurosis, the type of the neurosis depending on the gene responsible.

Neurosis would then become a congeries of qualitatively distinct syndromes. With adequate knowledge of the differentiæ of neurotics, we would be able to sort them out from the remainder of the population, who would be immune to neurosis; we would also be able to sort out the neurotics into their various classes. In the family histories of neurotics, we would expect to find that the specific forms of neurosis characteristic of the propositi occur with exceptional frequency, but that other forms of neurosis occur with no greater frequency than in the general population. We would also expect that the frequency with which neurotic abnormalities occur would bear no necessary relation to the extent to which these abnormalities deviate from the norms of the general population. The available evidence is against these expectations. Persistent search for characteristics which will clearly discriminate between different types of neurotics and between them and normals has so far proved fruitless. Not only specific, but also non-specific forms of neurosis are commoner among the relatives of neurotic propositi than in a control group. To substantiate this last point we may quote the evidence provided by Brown (1942).

This observer investigated the frequency of various types of psychiatric abnormality among the parents and sibs over the age of fifteen of different groups of neurotic propositi. From the data provided by him the following table can be constructed:

Numbers of	Among Parents and Sibs of			
	Anxiety Neurotics	Hysterics	Obsessionals	Controls
Anxiety neurotics	55	7	3	—
Hysterics ..	7	12	—	2
Obsessionals ..	2	—	7	—
Depressives ..	9	—	4	—
Abnormal personalities ..	60	10	24	19
Other psychiatric abnormalities	22	9	2	4
Normal ..	199	69	56	160
Totals ..	354	107	96	185

We may observe, among the relatives of the three groups of propositi, the incidence of the non-specific anomalies, i.e. everything but anxiety neurosis among the relatives of the anxiety neurotics, everything but hysteria among the relatives of the hysterics, etc., and compare them with the corresponding incidences in the control group. In this way we obtain the following figures:

	X^2	Degrees of freedom	Probability
Anxiety group ..	26·363	5	$<$·01
Hysterical group ..	22·249	3	$<$·01
Obsessional group	30·418	5	$<$·01
Totals ..	79·030	13	$<$·01

In other words it may be asserted with a high degree of certainty that the relatives of all three neurotic groups of propositi distinguish themselves from normals by an excessive liability to other psychiatric abnormalities than the specific ones in question.

We are therefore led to consider an alternative form of the third hypothesis. According to this, the genetic determinants which produce a neurotic constitution are generally non-specific and additive in their effects. Each operates to produce a reduced resistance to some kind of stress; and in their endless combinations, they facilitate the occurrence of a wide variety of neurotic states, in which phenomena symptomatic of one type of diagnosis may overlap with those symptomatic of others. This theory again leads to a number of expectations, which can be compared with observed facts.

In summary, theories of neurosis seem capable of being classified in three main categories:—

(i) Those which imply that the causes of neurosis are wholly exogenous.

(ii) Those which postulate a unitary endogenous factor determining variations in susceptibility to neurosis; it may be either:

(*a*) A single abnormal gene.

(*b*) A large number of separate genes of small but similar effect.

(iii) Those which assume more than one genetic factor, with dissimilar effects, to account for the neurotic constitution. They may either:

(*a*) be specific to a particular type of neurosis;

(*b*) overlap in their effects and produce predispositions to more than one type of neurosis.

Many of the phenomena of neurosis are compatible with more than one of these hypotheses, and may be observed without provoking any explicit choice (though a choice is often involved by implication in the interpretation placed on neurotic phenomena). There may be advantages, however, in choosing a particularly promising hypothesis, even before it can be claimed to be the only possible one, and seeing where it leads us. The one we have chosen belongs to class (iii) (*b*). A general and a precise formulation follow, together with evidence to explain our choice.

The Proposed Theory

A very large number of characteristics may be differentiated among men, each of which plays a part in determining the success with which the individual adapts to circumstances. We can define each of these characteristics in such a way that the possession of it promotes success and lack of it promotes failure. In these terms our theory is that the normal man possesses certain characteristics and lacks others in roughly equal proportions; the man with neurotic tendencies, on the other hand, lacks many and possesses few. Although he may not be found abnormally lacking in any particular characteristic, the consequence of his being lacking in many is that he is more than averagely prone to be unsuccessful in his adaptations, and to relapse in consequence into neurotic symptoms. Thus a man with neurotic tendencies may be no more lacking in characteristic A than many men whose adjustments are normal; but he may also lack characteristics B, C, D, and E, of which men who lack A normally lack only one or two. Another man with neurotic tendencies may not be lacking in A or B, but may lack C, D, E, and F. Thus, although he falls into the same broad class, of men prone to neurosis, his personality may present a different picture, and the conditions which induce him to break down and the symptoms he then develops may all be different.

In more precise terms, every individual possesses characteristics variable in strength which render him more or less liable to a neurosis of any kind. Whether he succumbs to a neurosis of a particular kind or not depends on the extent to which he is endowed with characteristics which help to confer immunity to that kind of neurosis, and on the nature and the degree of the stresses to which he is exposed. We do not wish to suggest that all these characteristics are entirely endogenous or genetically determined.

In the general population each of these characteristics may be considered as normally distributed, so that their collective distribution may be visualized as a normal surface in many dimensions. This multivariate frequency ellipsoid is exposed to a series of stresses of different degrees coming from different directions, which have the effect of partitioning it in various ways. Each particular stress divides the population into two classes—those who withstand it and those who succumb. The apparent qualitative distinction between neurotics and normals is the resultant of a balance between two quantitatively variable forces. When stress exceeds resistance, the man becomes classifiable as neurotic, when resistance exceeds stress, as normal. Both stress and resistance vary in degree.

But both vary also in kind. Some people may be so feebly endowed in all relevant characteristics that they may succumb to almost any stress, provided it is sufficient in degree. A particular stress, if sufficient, will produce symptoms of neurosis in these people, but may also find out the Achilles heel in others who would have been immune to any equally severe stress coming from a different direction.

We present this as a heuristic hypothesis, i.e. not as one which can be either finally proved or disproved on existing or readily accessible evidence, but as one which may prove useful for experimental purposes. Any satisfactory theory of neurosis is more likely to be reached rapidly and established soundly, we believe, if the implications of the proposed theory are explored than if they are ignored.

Why is it likely to be useful? Arising from genetic considerations, it offers an account of the relationship between normal and abnormal psychological phenomena and therefore extends the range of observations which students of either branch of psychology can take into account. In particular it relates the problems of psychiatry to the general concept of human variability which has been developed by psychometric psychology, and which again is related to the system of applied logic which has been found suitable for the biometric sciences as a whole. It therefore places at the disposal of psychiatry the scientific techniques, particularly those of statistical analysis which have been developed for the biometric sciences by Galton, Pearson, Fisher, and others. These practical advantages are sufficient, in our opinion, to justify asking for a trial of the theory.

Some of its corollaries may be suggested as suitable for study:

1. (Also reconcilable with theories of types (i) and (ii) (*b*).) Neurotics, by hypothesis, are obtained from the normal population by a process of selective sampling, and are therefore a sub-class of normal men. If so, in the observation of any particular characteristic, neurotics will be found to fall within the limits of range of the general population, and will not occur in excessive numbers at a particular extreme.

2. (Also reconcilable with types (i) and (ii) (*b*).) When unselected groups are submitted to environmental stress of varying degrees, the numbers of persons breaking down will increase with the intensity of the stress, and no final end-point will be found at which all have broken down who are ever liable to. The relationship between degree of stress and frequency of breakdown will be positive, but of limited extent because:

3. (Also reconcilable with (iii) (*a*).) Certain types of stress will be particularly likely to produce breakdown among particular types of people, e.g. acute physical danger and uncertainty among persons liable to anxiety states, positions of grave responsibility among those of obsessional types, etc. This relationship will also be limited in extent, since people are affected by the degree of a given stress as well as the direction from which it comes.

4. Conversely, it should be possible to assess the liability of different individuals to neurosis generally and to neuroses of different kinds specifically. Those who break down under the least degrees of stress should be found the most heavily loaded with "negative" characteristics, as earlier defined.

5. (Also reconcilable with type (i).) Mixtures of characteristics, and therefore mixtures of symptoms, will occur more frequently among neurotics than pure types.

6. (Also reconcilable with (iii) (*a*).) Neurotics will be found heterogeneous.

7. Among relatives of propositi suffering from a given type of neurosis, the incidence of neuroses of other kinds should be higher than among the normal population.

If satisfactory evidence can be adduced on all these points, we shall consider our theory confirmed, since, taken together, they are irreconcilable with a theory of any other type than (iii) (*b*).

Evidence Relevant to the Choice between Possible Theories

Evidence has already been quoted from other sources in the discussion of possible theories above, which is sufficient, for instance, to exclude theories of type (i); and other evidence published by Slater (1943) corroborates every expectation listed above except 1, on which no data were available. Other sources might be cited. But investigations conducted at Sutton Emergency Hospital during 1942–44 provide fresh unpublished evidence which is presented and discussed below.

In one experiment, six tests used by the Army for selecting personnel were given to enough serial weekly intakes at the hospital to provide a sample of 200 men: four were tests of mental abilities (general intelligence, verbal, arithmetic, and mechanical abilities) and two of physical abilities (agility and auditory acuity). The patients proved to have the same average age as men in the serving army, and reached the same average scores on the tests of mental abilities. Their agility was found to be lower and their auditory acuity poorer. The correlation between their results on these two tests is +0·3307, which is significantly higher than the corresponding correlation in the normal serving army, +0·1004 (on 2,600 cases).

Several hypotheses might account for these findings, among them the hypothesis that neurotics tend to be constitutionally inferior. This belongs to type (ii) (*b*): the fact that neurotics' agility is relatively poor is related hypothetically to the fact that their auditory acuity is also relatively poor, and a general common cause is supposed. If there is one, it should produce other effects, and appear, for instance, in other physical abilities. This was tested. The next 200 men in following intakes were given a test of visual acuity. They proved to have significantly poorer vision than men tested in the serving army, and significantly more of them wore glasses.

The hypothesis therefore appeared confirmed. It also agreed with previous results (Slater, 1943) which showed by factor analysis that positive family history, childhood neurosis, poor work record, previous nervous breakdown and abnormal personality are all interrelated phenomena among neurotics, and that their interrelations can be accounted for as manifestations of a common underlying characteristic, the neurotic constitution.

But there is nothing in this evidence which excludes our proposed theory. If we take a random sample of the population, we shall expect not only to find some men deficient in auditory acuity, but also, among these, some who are deficient in agility, and finally, among these, some who are also deficient in visual acuity. Our theory, in this instance, is simply that those who happen to be deficient in two or three abilities are those most likely to find their way into a neurosis centre. This accounts for the observations as adequately as the hypothesis of a single common factor.

There is, moreover, a point at which the evidence accords only apparently with the single factor theory, and in fact conflicts with it; and where the consideration of our theory provokes a closer inspection of the evidence and reveals the importance of facts which might have been overlooked. This contradictory evidence is that the correlation between the auditory acuity and agility tests is higher among neurotics than among normals. If both defects are manifestations of a neurotic constitution, and this is a unitary trait, the neurotics, who are alike in respect of it, should also be relatively homogeneous as regards the defects. But homogeneity lowers the correlation between associated variables (Thomson, 1939); so the proportions of the two correlations should have been reversed.

This leads us to compare variances in performance on the two tests among neurotics and normals. The mean square variance on the agility test is 4·39 times as great among neurotics as among normals (5,000 cases), and on the auditory acuity test at least 1·19 times as great (2,600 cases: but this test is not so sensitive to degrees of acuity above average as below). Although neurotics are supposed alike as regards neurotic constitution, and this is supposed to affect their test results on both tests, they are found, in fact, abnormally heterogeneous. When the correlation between their results is corrected for heterogeneity (Thomson, 1939), it is reduced to +0·1676, which does not differ significantly from the normal value. Further corroboration is provided by the visual acuity test, on which the mean square variance of neurotics is 3·03 times that of normals (2,233 cases).[1]

These observations suggested that further evidence on heterogeneity might be found if sought for. Qualitative findings differ in frequency among the different classes, as already shown (Slater, 1943); but heterogeneity can also be demonstrated quantitatively. The alphabetically arranged card index of the admissions to all military neurotic wards of the Hospital from the beginning of the war until January, 1944, were searched for persons with a diagnosis, or part diagnosis, of obsessional state: 113 of these were found. The next card lying to that of each of these was taken for a miscellaneous group, and the succeeding cards were searched for the nearest name with a diagnosis of anxiety state, hysteria, and reactive depressive state. Five groups, each of 113 persons, were so obtained by a strict method of random selection, and the relevant data are:

Diagnostic group	Mean age in years
Obsessionals	28·64
Miscellaneous	29·25
Anxiety neurotics	29·07
Hysterics	28·89
Reactive depressives	31·69

* Full particulars are on record at the War Office.

The reactive depressives appear older than the others. A precise test shows that the difference is significant:

Source of variance	Sum of squares	Degrees of freedom	Mean square
Total variance in age	25506·21	564	—
Variance between depressives and others	672·66	1	672·660 [1]
Remaining variance between groups	23·05	3	7·683
Variance within groups (error) ..	24810·50	560	44·304

[1] $F = 15{\cdot}183$ $P < 0{\cdot}01$

Note.—S.D. of age within groups = root mean square variance = 6·656 years.

The remaining groups do not differ significantly from one another, nor, for that matter, from the larger group of which they form a sample.

Scores of many of these patients on intelligence tests are kept, and were inspected for evidence of heterogeneity: the same procedure was followed. Different tests were in use at different periods. Records were sufficient to enable 300 patients to be classified in 12 groups of 25 according to diagnosis and test given. The diagnoses were the first four given above, and the tests used, Progressive Matrices, Shipley Vocabulary, and Cattell Intelligence Tests II, *a*. They show that obsessionals score significantly higher on intelligence than others, but that anxiety neurotics and hysterics do not differ significantly from each other or from the miscellaneous group (Slater, P., 1944).

Other data collected at the hospital by Miss E. Bennett, but not yet published, show that psychopaths are heterogeneous in their reaction times under free-association tests (2,400 times recorded).

Thus when age is considered, the heterogeneity of neurotics is demonstrated by the difference between reactive depressives and others; when intelligence is considered, heterogeneity is demonstrated by the difference between obsessionals and others; and heterogeneity is found among psychopaths when reaction times are measured. The accumulation of evidence demonstrating the heterogeneity of neurotics is considerable, and might be held sufficient to exclude theories of type (i) or (ii).

Evidence of a different kind is required to differentiate between theories of type (iii) (*a*) and (iii) (*b*). If the former is correct, neurotics must be treated as qualitatively distinct from normals; this would become necessary if it could be shown that some characteristics are present among neurotics which are entirely absent among normals, or that the absolute frequency with which abnormal degrees of certain characteristics occur among neurotics is too great to be treated as a random deviation from norms appropriate to the general population.

It is therefore important to arrive at the best possible estimate of the incidence of neurosis under the circumstances with which we have to deal at present. From the most complete information available, we estimate that the odds are about 65:1 against a man being referred to hospital for the treatment of a neurosis during a year's service in the army.

Let us apply this estimate to another criterion of neurotic tendency. In an experiment carried out by Miss Elizabeth Bennett at Sutton Emergency Hospital, lists were prepared of 100 things men might disapprove of, 100 that might make them nervous or afraid, and 100 that they might enjoy. This is an adaptation of the Pressey Cross-Out Test. It was given to 80 normal men and to 160 patients from the neurotic wards, of whom 80 were classified as neurotic and 80 as psychopathic. It was found that neurotics and psychopaths alike tended to disapprove of more, to be afraid of more, and to enjoy fewer things than the normals. An analysis of the answers suggests that the test functions as a measure of inadequacy. When the separate sections are appropriately weighted, neurotics and psychopaths tend to obtain negative scores, and normals positive ones. The overlap between the two groups is 26 per cent. We can estimate that the correlation between test result and neurotic tendency is +0·5, and this is about as high as we can expect to obtain with any single test.

How much use is such a test as a diagnostic instrument? If neurotics and normals were two divergent types, and occurred in equal numbers, like males and females, we could differentiate them from each other correctly in 74 per cent. of our cases. But we have estimated that the odds against an unknown man developing a neurosis within a year are 65:1. So even if his score is an unusual one for a normal man, and a common one for a neurotic, the odds may still be in favour of his being normal, at least for an operationally effective period. In point of fact, if a man obtains the average score for a neurotic, the odds against his developing a neurosis are 13:1. Even if his score is so low that only 1 per cent. of neurotics score lower, the odds are only even that he will develop a neurosis within a year. The whole neurotic group falls within the normal group (i.e. those in an apparently normal state at a given time), when we take into account the relative sizes of the two groups.

As another instance, we might consider the use of the electroencephalogram as an index of abnormality. This test is ordinarily used to supplement a diagnostic opinion which carries its own independent weight. In treating the evidence of the test in isolation, we do not wish to be taken as implying any criticism of diagnostic opinions it has been used to supplement. In the average population the incidence of abnormality of E.E.G. is believed, on estimates available, to be approximately 10 per cent. In various types of the psychiatrically abnormal this frequency rises to any figure up to 90 per cent.; for a general neurotic group it has been given as approximately 25 per cent. Then if one man in 66 is liable to neurosis within a year, one in 79 of those with normal E.E.Gs. is so liable, and one in 26 of those with abnormal E.E.Gs. Let us, however, take a much larger estimate of the frequency of

"neurosis." It has been suggested that about 10 per cent. of the population exhibit neurotic or psychopathic traits (that they exhibit them in some degree is readily admissible on our hypothesis). Then of those with normal E.E.Gs. one in twelve will be neurotic, and of those with abnormal E.E.Gs. one in four. In this case, as in the foregoing, one of a psychological test, the range of the neurotic group falls within the range of the normal, and no clear-cut qualitative distinction appears.

This evidence is only sufficient to illustrate the difficulties that are likely to be encountered in attempting to establish a theory of type (iii) (*a*), and the necessity of carrying out adequate control experiments among normals before any criteria are accepted as valid for differentiating neurotics. Ideally, if a theory of type (iii) (*a*) can be established, an exact classification of cases should be possible, into normals and neurotics of different varieties. If we prefer a theory of type (iii) (*b*), we are not obliged to suppose that neurotics cannot be differentiated from normals or from one another. But our approach to this problem and our method of formulating conclusions will be different. By selecting a fairly large number of characteristics for measurement which are relatively independent of one another and which are more noticeable among neurotics than normals, and applying methods of weighted summation (e.g. by computing discriminant functions) we may be able to measure the probability that an individual may develop a neurosis, and grade people for relative liability or immunity (which may approach certainty of one kind or another in certain cases). Our main reason for preferring a theory of this type is that we believe it provides the more promising approach at the present time. A weighted summation of ten tests tried out by Miss Bennett, including the three sections of the adapted Pressey X–O test already mentioned, provides a range of scores on which the probability of neurosis rises from less than 0·001 to over 0·99 (taking into account the estimate of the incidence of neurosis already given). Up to 20 per cent. of the population can be classed in the former category; while a bottom 2·2 per cent. can be differentiated, amongst whom 61·4 per cent. of the neuroses can be expected to occur.* The interpretation of observations according to our theory has therefore led to promising results.

Summary

Possible theories of the nature of the neurotic constitution are considered, together with their consequences in statistical expectations of various kinds. A theory is proposed, which is held to accord best with the relevant data available at present, and which has heuristic value in providing a scheme of attack on the genetic problems of psychopathy, and in rendering available to psychiatry the techniques of statistical analysis which have been found suitable to the biometric sciences. According to this theory, the neurotic constitution is preponderantly determined by a very large number of genes of small effect. The effects of these genes, at least in so far as they are qualitatively similar, may be additive; and they become manifest by producing a reduced resistance to some form of environmental stress, and so facilitate the appearance of a neurosis. In so far as the effects of the genes are qualitatively dissimilar, the type of stress effective in producing breakdown, and the neurotic symptoms produced, will tend to differ. The neurotically predisposed man is then to be regarded as a man who has a more than average susceptibility to environmental stresses of one or a number of kinds; he represents one of the extremes of normal human variation.

* Results from 80 normal and 80 neurotic patients. A report on this experiment is being prepared for publication.

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BOOK REVIEWS

PARANORMAL COGNITION

L. J. Bendit

(Faber & Faber, London, 1943. Pp. 79. 5*s*.)

The author adopts as a working assumption the hypothesis that the existence of extra-sensory perception has been proved beyond reasonable doubt. He discusses the different mental states in which these phenomena occur, contrasting the alert, critical attitude encouraged by Rhine in his experiments, with the dissociated, hysterical states in which comparable material is produced by mediums, people who are drugged or ill, etc. He points out that patients attending a doctor for psychotherapy may also produce symptoms or ideas which can be interpreted along these lines, and illustrates this by a series of examples from his own practice and non-professional experience. When the true nature of these symptoms is realized and explained, benefit to the patient results. The author considers that extra-sensory perception is, at least, very common both in man and in animals, and that it is probably to be associated with the sympathetic nervous system. As a rule protopathic, it may be lifted to an epicritic level. If neglected, these functions may become regressive and potentially morbid; an increasingly conscious control and integration with other functions are to be aimed at.

LANGUAGE AND THOUGHT IN SCHIZOPHRENIA

J. S. Kasanin

(University of California Press, 1944. $2.00. Pp. 133)

This small book contains material likely to give thought to all interested in the symptomatology of schizophrenia. The papers are all by authorities and each has contributed to the book. It is to be recommended to those interested in the abnormal cerebral processes encountered in this field of psychiatry.

ENGLETON'S INDEX AND ABSTRACTS OF LITERATURE ON PROGRESS IN INTRACRANIAL LESIONS RELATED TO AURAL AND NASAL CONDITIONS.

(Limited Edition, 1941)

This is a substantial volume of some 500 pages. Its substance is provided by a number of reviews of world literature on intracranial complications of aural and nasal sepsis. The reviews were originally published in the Archives of Oto-laryngology. They cover, with some interruptions, the period 1925–1940 and are here fully reprinted. The subject is widely and satisfactorily covered, and the index should prove a most valuable reference volume. A feature of the work is a very full subject index.

NARCOANALYSIS

J. Stephen Horsley

(Oxford Univ. Press, London, 1943. Pp. 134. 8*s*. 6*d*.)

The purpose of this book, says the author in his preface, is to describe a technique which he has devised in order to shorten the course of deep mental analysis and psychotherapy. The patient, drugged by barbiturate, talks freely and repressed, forgotten or withheld episodes of his history are made known to the observer. The information thus acquired is subsequently used in attempts to integrate the psyche.

The account of the method and of the results obtained is obscured by more or less relevant psychiatric jottings, and by random quotations from other authors. The structural formulæ of some of the barbiturates are given. There is the inevitable collection of dreams and a short chapter on malingering. It is a pity that Dr. Horsley has not supplemented the introduction of his valuable method of treatment by a pertinent and lucid description of its value and limitations.